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-To my family

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Abbreviations

ACEi	Angiotensin converting enzyme inhibitor
ACS	Acute coronary syndrome
ANOVA	Analysis of variance
ARB	Angiotensin II receptor blocker
ASA	Acetylsalicylic acid
BMI	Body mass index
BP	Blood pressure
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CI	Confidence interval
CONSORT	Consolidated standards of reporting trials
CROS	The Cardiac Rehabilitation Outcome Study
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DM	Diabetes mellitus
EAPC	European Association of Preventive Cardiology
eGFR	Estimated glomerular filtration rate
ESC	European Society of Cardiology
EUROASPIRE	European action on secondary and primary prevention by intervention to reduce events
EQ5D	EuroQol- 5 Dimension Scale
ExCR	Exercise-based cardiac rehabilitation
HbA1c	Haemoglobin A1c
HDL	High-density lipoprotein

LDL	Low-density lipoprotein
MI	Myocardial infarction
NACR	National Audit of Cardiac Rehabilitation
NIPALS	Non-linear iterative partial least squares
NSTEMI	Non-ST elevation myocardial infarction
OGTT	Oral glucose tolerance test
OPLS-DA	Orthogonal partial least squares discriminant analysis
PCI	Percutaneous coronary intervention
Perfect-CR	Perfect cardiac rehabilitation
PLS	Partial least squares
PREDIMED	Prevención con Dieta Mediterránea
RCT	Randomized controlled trial
SCORE	Systematic Coronary Risk Estimation
SD	Standard deviation
SE	Standard error
SMART	Second manifestations of arterial disease
STEMI	ST elevation myocardial infarction
SWEDEHEART	Swedish web-system for enhancement and development of evidence-based care in heart disease evaluated according to recommended therapies
SBP	Systolic blood pressure
UA	Unstable angina
UK	United Kingdom
USA	United states of America
VIP	Variables of importance for the projection
W	Watts
WHO	World Health Organization

Sammanfattning på svenska

Hjärt-kärlsjukdomar är den största orsaken till sjukdom och död i Sverige och i världen idag. År 2015 uppskattades det att över 85 miljoner européer levde med hjärt-kärlsjukdom. Hjärt-kärlsjukdomar innefattar bland annat kranskärlssjukdom, perifer kärlsjukdom och stroke, som orsakas av åderförkalkning. Vid åderförkalkning leder inflammation till fettansamling och kalkavlagring i kärlväggar vilket leder till förträningar av kroppens blodkärl. Åderförkalkning ger till en början inga symtom. Symtomen uppkommer först när fettsamlingen leder till kärlförträngningar och begränsat blodflöde, eller till en propp som orsakar totalstopp i blodflödet. Om åderförkalkningen sker i kranskärlen kallas det för kranskärlssjukdom, vilket är den bakomliggande orsaken till hjärtinfarkt. Vid en hjärtinfarkt hindras blodtillförseln till hjärtmuskeln och hjärtat tar skada av syrebristen. Vården av hjärtinfarktpatienter har utvecklats mycket under det sista seklet, från att bestå enbart av sängvila under flera veckor, till dagens läkemedelskombinationer och ingrepp. Denna utveckling har medfört att överlevnaden efter hjärtinfarkt har ökat markant.

Efter att man har drabbats av en hjärtinfarkt är risken för att få ny hjärtinfarkt hög. Sekundärprevention handlar om de förebyggande åtgärder som sätts in efter en första hjärtinfarkt, för att förhindra nya hjärtinfarkter. Sekundärprevention efter hjärtinfarkt ges i form av hjärtrehabilitering, och innebär att man försöker reducera de riskfaktorer som driver på åderförkalkningsprocessen. Vissa riskfaktorer kan man inte påverka, till exempel ålder. Studier har dock visat att hjärtinfarkter orsakas till störst del av modifierbara riskfaktorer såsom rökning, diabetes, höga blodfetter, högt blodtryck, fysisk inaktivitet och dålig kosthållning. Hjärtrehabilitering är ett allsidigt program där kardiologer, specialiserade sjuksköterskor och fysioterapeuter arbetar i team med medicinskt omhändertagande, handledd träning, livsstilsförändringar och psykosocialt stöd för hjärtinfarktpatienter. Hjärtrehabilitering har en stark forskningsbas där flera studier har visat att återinsjuknande och död kan förebyggas. Tyvärr har andra studier visat att hjärtrehabilitering inte används optimalt och att patienter inte uppnår behandlingsmål i tillräckligt stor utsträckning.

Med delarbeten i denna avhandling ville vi dels undersöka vilka tjänster erbjuds inom svensk hjärtrehabilitering och dels studera nya arbetssätt som potentiellt kan leda till förbättringar inom hjärtrehabilitering. Avhandlingen består av fyra delarbeten som handlar om evaluering och förbättring av hjärtrehabilitering.

Delarbete I genomfördes på hjärtrehabiliteringsenheten vid Skånes Universitetssjukhus i Malmö. Där inleddes sjuksköterskeledd individanpassad hjärtrehabilitering vilket innebar förändringar i hur man följde upp patienter efter att de drabbats av hjärtinfarkt. Innan förändringen (traditionell hjärtrehabilitering) hade hjärtrehabiliteringsenheten patientansvar i tre månader. Patienterna fick under denna period träffa sjuksköterska vid ett tillfälle och läkare vid ett tillfälle. Därefter remitterades patienterna till sin lokala vårdcentral för fortsatt uppföljning. Sjuksköterskeledd individanpassad hjärtrehabilitering innebar följande förändringar: programmet utökades till ett år och en sjuksköterska blev huvudansvarig för patienterna genom hela programmet; man gjorde en individuell bedömning om huruvida patienterna behövde träffa läkare; man tog extra blodprover vid 6 månader och ringde upp de som hade rubbade blodvärden; och man skickade brev till patienterna vid 6 månader med tips och råd om livsstilsförändringar. I delarbete I jämfördes en grupp patienter som deltagit i traditionell hjärtrehabilitering (totalt 105 patienter) med en grupp som deltagit i den sjuksköterskeledda individanpassade hjärtrehabiliteringen (totalt 112 patienter). Resultatet var att de patienter som deltagit i den sjuksköterskeledda individanpassade hjärtrehabiliteringen hade bättre blodtryck och blodlipidvärden ett år efter sin hjärtinfarkt. Färre patienter behövde träffa läkare, vilket innebar att man kunnat omprioritera läkarbesök till andra behövande patienter. Det blev under uppföljningsperioden fler telefonkontakter till sjuksköterska men antalet fysiska besök till sjuksköterska var detsamma. Konklusionen av studien blev att det nya arbetssättet gagnade hjärtinfarktpatienterna och arbetssättet behölls.

Delarbete II var en enkätstudie. Syftet var att undersöka arbetsrutiner på hjärtrehabiliteringsenheter i Sverige och inventera vilka tjänster de erbjöd. En grupp experter inom hjärtrehabilitering satte ihop en enkät bestående av 120 frågor. Frågorna var baserade på europeiska riktlinjer för hjärtrehabilitering och syftet var att se hur väl vi i Sverige håller oss till dessa. Enkäten skickades ut elektroniskt till alla 78 hjärtrehabiliteringsenheter i Sverige knutna till det svenska kvalitetsregistret, SWEDEHEART. Alla enheter svarade på enkäten och resultaten visade att hjärtrehabilitering i Sverige höll en hög standard jämfört med våra europeiska motsvarigheter. Till exempel erbjöds hjärtrehabilitering i stor utsträckning inom rekommenderad tidsram och nästan alla program hade rätt personal i sina team (läkare, sjuksköterska och fysioterapeut). En majoritet av programmen erbjöd individuella bedömningar hos en fysioterapeut och hade ett välutvecklat träningsprogram. Det fanns några områden där det fanns potential till förbättring såsom att ha en medicinskt ansvarig läkare för programmen, att ha regelbundna team-möten och att ha ett mer standardiserat innehåll i ett första patientbesök hos sjuksköterska. Flera enheter som deltog har fått återkoppling för att se hur deras verksamhet såg ut jämfört med resten av Sverige och många har deltagit i workshops med syfte att lära av varandra och förbättra den egna verksamheten till följd av studien.

Delarbete III var en så kallad randomiserad kontrollerad studie, vilket är en metod som används för att studera effekten av en behandlingsmetod i förhållande till en annan redan vedertagen sådan. Att studien är randomiserad innebär att studiedeltagarna slumpmässigt delas in i två grupper. För att kunna jämföra behandlingsmetoder behandlas den ena gruppen med den nya behandlingsmetoden och den andra gruppen med den redan vedertagna. I delarbete III jämfördes effekten av hjärtrehabilitering där en web-baserad applikation användes som ett komplement till traditionell hjärtrehabilitering, med enbart traditionell hjärtrehabilitering. Applikationen var speciellt designad för att komplettera hjärtrehabilitering och användarna skulle mata in till exempel vad de åt, hur mycket de rörde på sig, om de rökte och intag av mediciner. Totalt 150 studiedeltagare delades upp slumpmässigt i två grupper. En grupp fick traditionell hjärtrehabilitering och en grupp fick traditionell hjärtrehabilitering samt tillgång till applikationen. Tanken var att applikationen främst skulle påverka användarens livsstil, inklusive ökad fysisk aktivitet. För att utvärdera detta genomfördes ett cykeltest. Det visade sig att båda grupperna förbättrade sina cykeltestutfall under studiens gång och det gick inte att påvisa att applikationsgruppen gjorde bättre ifrån sig. Andra riskfaktorer för hjärt-kärlsjukdom jämfördes också och det visade sig att applikationsgruppen fick bättre blodtryck och bättrade sin kosthållning mer i studiens början. Konklusionen blev att en applikation som tillägg till hjärtrehabilitering kan vara ett bra verktyg för att behandla riskfaktorer men den optimala användningen behöver utforskas vidare.

I **delarbete IV** var syftet att undersöka vilka av organisationernas och patienternas egenskaper som kunde prediktera om patienter uppnådde behandlingsmål ett år efter hjärtinfarkt. Behandlingsmålen som studerades var LDL-kolesterol, ibland kallad för det ”onda” kolesterolet (under 1.8 mmol/L), blodtryck (under 140/90 mmHg) och rökstopp (självrapporterat). I denna studie användes resultaten av enkäten i delarbete II för organisatoriska egenskaper, kvalitetsregistret SWEDEHEART och Statistiska Centralbyrån för patientrelaterade egenskaper. Alla 9165 patienter som hade drabbats av hjärtinfarkt år 2016 i Sverige inkluderades i studien. Resultaten visade att ungefär hälften av de organisatoriska egenskaperna visades kunna prediktera att patienterna uppnådde behandlingsmål för LDL-kolesterol och blodtryck medan enbart 7% kunde prediktera rökstopp. Mått på tidigare hälsa (till exempel LDL-kolesterol och blodtryck vid insjuknande) var viktiga prediktorer för att uppnå behandlingsmål för LDL-kolesterol respektive blodtryck. För rökstopp var patientrelaterade egenskaper av större vikt, där patienter med hög ålder, tidigare hjärtsjukdom och låg socioekonomisk status var oftare aktiva rökare vid studiens slut. Att ha deltagit i träning som en del av ens hjärtrehabiliteringsprogram predikterade alla tre utfall positivt. Studien är viktig för att kunna kartlägga vilka delar man skall fokusera på vid organisering av hjärtrehabiliteringsprogram och forska vidare på i framtiden.

Samantekt á íslensku

Hjarta- og æðasjúkdómar eru algengustu sjúkdómarnir á heimsvísu og valda í dag flestum dauðsföllum. Árið 2015 var áætlað að yfir 85 milljónir Evrópubúa væru með hjarta- og æðasjúkdóma. Hjarta- og æðasjúkdómar eru meðal annars kransæðasjúkdómur og heilablóðfall, og orsakast af svokallaðri æðakölkun. Við æðakölkun leiðir bólga í æðaveggjum til fitusöfnununnar og kölkunar. Æðakölkun gefur upphaflega engin einkenni. Einkenni koma aðeins fram þegar fitusöfnun leiðir til þrenginga í æðum og takmörkunar á blóðflæði eða þegar blóðtappi leiðir til þess að blóðflæðið stöðvast algerlega. Þegar þetta gerist í kransæðum er það kallað kransæðastífla og hjartaáfall. Við hjartaáfall minnkar blóðflæði til hjartavöðvans og hann skaðast vegna súrefnisskorts. Meðhöndlun við hjartaáfalli hefur þróast mikið á síðustu öld, allt frá því að vera einungis nokkrar vikur í hvíld til fjölda lyfja og inngripa sem notuð eru í dag og hefur þessi framþróun aukið lífslíkur verulega.

Þeir sem eitt sinn hafa fengið hjartaáfall ertu í mikilli hættu á að fá aftur hjartaáfall. Til þess að fyrirbyggja nýtt hjartaáfall er sjúklingum ráðlagt að taka þátt í hjartaendurhæfingu sem felur í sér að taka á áhættuþáttum sem knýja áfram æðakölkunarferlið. Ekki er hægt að hafa áhrif á alla áhættuþætti, eins og til dæmis kyn og aldur, en rannsóknir hafa sýnt að hjartaáföll orsakast að miklu leyti af breytanlegum áhættuþáttum eins og reykingum, sykursýki, hárri blóðfitu, háum blóðþrýstingi, kyrrsetu og lélegu mataræði. Hjartaendurhæfing er heildrænt prógram þar sem hjartalæknar, sérhæfðir hjúkrunarfræðingar og sjúkraþjálfarar starfa saman í teymum sem veita einstaklingsbundna lyfjameðferð, ráð um hreyfingu og lífsstíl, sem og sálfélagslegan stuðning. Fjöldi rannsókna hafa sýnt fram á að hjartaendurhæfing kemur í veg fyrir endurtekin hjartaáföll og dauðsföll. Því miður hafa rannsóknir einnig sýnt fram á að hjartaendurhæfing er vannýtt og að sjúklingar nái ekki markmiðum meðferðar í nægilegum mæli.

Fjórar rannsóknir eru kynntar í þessari doktorsritgerð. Þær höfðu það markmið að kanna hvaða þjónusta er í boði í sænskri hjartaendurhæfingu og að rannsaka ný vinnubrögð sem hugsanlega gætu leitt til aukinnar nýtingar hjartaendurhæfingar og að sjúklingar nái markmiðum meðferðar í auknum mæli.

Rannsókn I var gerð á dagdeild hjartaendurhæfingar á háskólasjúkrahúsinu í Malmö í Svíþjóð. Þar var einstaklingsmiðaðri hjartaendurhæfingu komið á laggirnar. Fyrir breytinguna var sjúklingum fylgt eftir í þrjá mánuði. Sjúklingar hittu hjúkrunarfræðing einu sinni og lækni einu sinni, í kjölfarið var send beiðni til

heilsugæslu til að halda eftirfylgni áfram. Eftir breytingu voru ný vinnubrögð eftirfarandi: hjúkrunarfræðingur bar nú aðalábyrgð á sjúklingum, sjúklingunum var fylgt eftir í eitt ár, einstaklingsmat var gert á því hvort sjúklingarnir þyrftu að hitta lækni, blóðprufa var tekin eftir 6 mánuði og hringt í þá sjúklinga sem höfðu óeðlileg blóðgildi, og að lokum var sent bréf heim til sjúklinganna eftir 6 mánuði þar sem minnt var á gildi lífsstílsbreytinga. Sjúklingahópur sem tók þátt í hjartaendurhæfingu áður en breytingarnar voru gerðar (alls 105 sjúklingar) var borinn saman við sjúklingahóp sem tók þátt eftir að breytingarnar voru gerðar (alls 112 sjúklingar). Niðurstaðan var sú að sjúklingarnir sem tóku þátt í nýrri einstaklingsmiðaðri hjartaendurhæfingu höfðu bætt blóðþrýsting og blóðfitugildi sín meira en viðmiðunarhópurinn eftir eins árs eftirfylgni. Færri sjúklingar í þeim hópi þurftu að hitta lækni sem þýddi hægt var að forgangsraða læknisheimsóknum til annarra meira þurfandi sjúklinga. Á meðan rannsókninni stóð jukust símaviðtöl við hjúkrunarfræðinga, meðan fjöldi tíma til hjúkrunarfræðings var óbreyttur. Niðurstaða rannsóknarinnar var að einstaklingsmiðuð hjartaendurhæfing gæti gagnast sjúklingum eftir hjartaáfall og vinnulaginu var haldið.

Rannsókn II var gerð með spurningakönnun. Þar var markmiðið að skoða allar hjartaendurhæfingardeildir í Svíþjóð og sjá hvaða þjónustu þær byðu upp á. Hópur sérfræðinga í hjartaendurhæfingu setti saman spurningalista með 120 spurningum. Spurningarnar voru byggðar á evrópskum ráðum og viðmiðum um hjartaendurhæfingu og tilgangurinn var að sjá hversu vel þeim er fylgt eftir í Svíþjóð. Spurningalistinn var sendur rafrænt til allra 78 hjartaendurhæfingardeilda í Svíþjóð. Allar deildir svöruðu könnuninni og niðurstöðurnar sýndu að í samanburði við evrópskar ráðleggingar er hjartaendurhæfing í Svíþjóð í háum gæðaflokki. Til dæmis var hjartaendurhæfing að mestu leyti boðin innan ráðlagðra tímamarka, næstum allir höfðu lykilstarfsfólk í sínu teymi, þ.e lækna, hjúkrunarfræðinga og sjúkraþjálfara. Meirihlutinn bauð upp á einstaklingsbundið mat hjá sjúkraþjálfara og var með vel þróað þjálfunarprógram. Það voru nokkur atriði sem þurfti að bæta, svo sem að hafa lækni í stjórnunarstöðu, hafa reglulega teymisfundi og hafa staðlað innihald í fyrstu eftirfylgni hjá hjúkrunarfræðingi. Deildirnar sem tóku þátt fengu síðan skýrslu um hvernig starfsemi þeirra leit út miðað við restina af Svíþjóð og nokkrar hafa tekið þátt í námskeiðum með það að markmiði að læra hvert af öðru og bæta eigin starfsemi vegna rannsóknarinnar.

Rannsókn III var svokölluð slembiröðuð samanburðarrannsókn sem er rannsóknarform til að kanna áhrif einnar meðferðaraðferðar samanborið við aðra hefðbundna aðferð. Slembiröðun þýðir að þátttakendum rannsóknarinnar er skipt af handahófi í tvo hópa sem síðan eru veittar mismunandi meðferðir. Tilgangur rannsóknar III var að meta áhrif vef-forrits (App) sem viðbót við hefðbundna hjartaendurhæfingu. Appið var sérstaklega hannað fyrir hjartaendurhæfingu þannig að sjúklingarnir gætu skráð och fylgst með mataræði, hreyfingu, reykingum og lyfjanotkun. Samtals 150 einstaklingum sem höfðu fengið hjartaáfall var skipt af handahófi í tvo hópa, einn hópur fékk hefðbundna hjartaendurhæfingu og hinn

hópurinn fékk hefðbundna hjartaendurhæfingu og aðgang að appi. Tilgátan var að appið myndi fyrst og fremst hafa áhrif á lífsstíl, og þannig meðal annars leiða til aukinnar hreyfingar. Var því valið að meta áhrif appsins með þolprófi. Það kom í ljós að báðir hóparnir bættu sig í þolprófi en ekki var hægt að sýna fram á að app-hópnum færi meira fram en hinum. Einnig voru aðrir áhættuþættir hjarta- og æðasjúkdóma rannsakaðir og í ljós kom að app-hópurinn bætti blóðþrýsting og mataræði í upphafi rannsóknarinnar meira en hópurinn sem fékk eingöngu hefðbundna hjartaendurhæfingu. Lokaniðurstaðan var sú að appið getur verið góð viðbót við hefðbundna hjartaendurhæfingu en rétt hlutverk þess þarf að rannsaka betur.

Í **rannsókn IV** var tilgangurinn kanna bæði skipulags- og stjórnarbreytur og sjúklingabreytur og sjá hvort þær gætu spáð fyrir um hvort sjúklingar næðu markmiðum meðferðar einu ári eftir hjartaáfall. Meðferðarmarkmiðin sem voru rannsökuð voru LDL kólesteról, stundum kallað „vonda kólesterólið“(undir 1,8 mmól/L), blóðþrýstingur (undir 140/90 mmHg) og reykleysi (sem sjúklingar kunngerðu sjálfir) einu ári eftir hjartaáfall. Í rannsókn IV var notast við niðurstöður könnunarinnar í rannsókn II fyrir skipulags-og stjórnarbreytur, og fyrir sjúklingatengdar breytur var notast við sænska gæðaskrá yfir hjartasjúkdóma og Hagstofu Svíþjóðar. Gögn 9165 einstaklinga sem höfðu fengið hjartaáfall árið 2016 í Svíþjóð voru notuð í rannsókninni. Niðurstöðurnar sýndu að um helmingur skipulags- og stjórnarbreyta gátu spáð fyrir um að sjúklingar næðu markmiðum meðferðar LDL kólesteróls og blóðþrýstings, en aðeins 7% spáðu fyrir um reykleysi. Breytur sem lýstu fyrri heilsu (til dæmis lágt kólesteról við upphaf veikinda og saga um háan blóðþrýsting) höfðu sterkt forspársgildi um að ná meðferðarmarkmiðum fyrir LDL kólesteról og blóðþrýsting. Þegar kom að reykleysi höfðu sjúklingabreytur meira vægi en skipulags- og stjórnarbreytur. Sjúklingar sem voru eldri, höfðu sögu um hjarta- og æðasjúkdóma og lága félags- og efnahagslega stöðu voru oftar virkir reykingamenn í lok rannsóknarinnar. Að taka þátt í þjálfun undir handleiðslu sjúkraþjálfara sem hluta af hjartaendurhæfingu var sterkur forspárþáttur fyrir að ná öllum þremur meðferðarmarkmiðunum. Rannsóknin er mikilvæg til að geta kortlagt á hvaða hluta á að einblína á við skipulagningu hjartaendurhæfingar og við frekari rannsóknir í framtíðinni.

Introduction

The definition and development of cardiovascular disease

Cardiovascular disease

Cardiovascular disease (CVD) is an umbrella term for various diseases affecting the heart and blood vessels. They include, for example, coronary artery disease (CAD), cerebrovascular disease and peripheral artery disease (1). On a cellular level, the pathology of CVD is mostly due to a process called atherosclerosis, caused by a combination of risk factors, many of which are modifiable with medication and behavioural modification (2).

CVD can affect multiple organ systems within the body. When it affects the coronary arteries, it is called CAD. The main clinical manifestation of CAD is myocardial infarction (MI), which occurs when atherosclerosis in the coronary arteries causes limited blood-flow leading to damage to the heart muscle. This thesis will focus on risk factor management in patients after suffering an MI.

Atherosclerosis

Atherosclerosis is a condition where fatty acids and/or fibrous material accumulate within arterial walls and cause chronic inflammation (2). It is a process that starts in early adulthood and continues at a different pace in different individuals based on individual risk factor burden and genetic disposition (2).

The arterial wall is made of three layers, the outermost tunica adventitia, the middle tunica media, and the innermost tunica intima (Figure 1). The intima is a single layer of endothelial cells supported by an elastic membrane. The endothelial cells cover the inside of the arterial lumen and are in direct contact with passing blood providing passage of nutrients from the blood through the arterial wall. A healthy endothelial cell layer is smooth and has an anti-thrombogenic role. The tunica media consist of smooth muscle cells and elastic material such as collagen and elastic fibres. The adventitia is an elastic membrane that surrounds the middle layer. It contains mast cells, nerve endings and blood vessels (vasa vasorum) supplying blood to the tunica media (2).

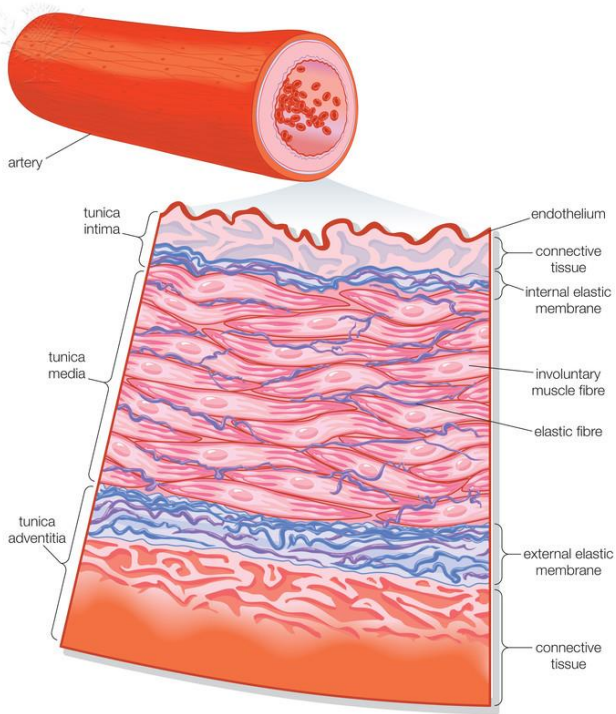

Figure 1. The layers of the arterial wall

The arterial wall consists of three layers. The innermost layer, the tunica intima composed of a simple squamous endothelial cell layer and a connective tissue layer, the tunica media composed primarily of smooth muscle cells, and, lastly, the tunica adventita composed of nerve endings, mast cells and blood vessels embedded in connective tissue. Reproduced with permission from Britannica Image Quest, ©Encyclopaedia Britannica.

An atherosclerotic plaque forms in the intima and progresses over time. Evidence suggests that initially low-density lipoprotein (LDL)-cholesterol accumulates and undergoes modifications rendering it pro-inflammatory and immunogenic (2). This leads to activation of endothelial cells and recruitment of circulating immune cells (monocytes, neutrophils, and T-cells). The immune cells enter the intima via adhesion molecules expressed by activated endothelial cells. Once inside, monocytes differentiate into macrophages that engulf the modified LDL-cholesterol, transforming into foam cells, the hallmark of an early atherosclerotic lesion. The accumulated immune cells in the arterial wall release inflammatory mediators, further activating endothelial cells and leading to increased endothelial permeability, production of more pro-inflammatory mediators and platelet aggregation, thus triggering a feed-back loop of chronic inflammation (2, 3).

The most widely accepted reason for the initiation of this cascade of chronic inflammation is that irritative stimuli such as elevated LDL-cholesterol, high blood pressure (BP), pro-inflammatory mediators, or turbulent blood-flow cause the

activation of endothelial cells (3, 4). The risk factors that accelerate the progression of the atherosclerotic process include hypertension, dyslipidaemia, tobacco smoking and diabetes mellitus (DM), which activate several points on the pathogenic pathway (3).

If atherosclerosis becomes advanced, it can narrow the arterial lumen limiting blood-flow to vital organs. Even atherosclerotic plaques which are not in themselves flow-limiting, can rupture and cause thrombus formation and obstruction of blood-flow leading to end-organ damage (2, 3).

Coronary artery disease

CAD is almost always caused by coronary atherosclerosis with or without luminal thrombosis (5). Clinically, CAD can manifest itself as stable angina pectoris or acute coronary syndrome (ACS).

The most common chronic manifestation of coronary atherosclerosis is stable angina (5). Stable angina usually presents as chest discomfort on exertion, alleviated by rest or nitroglycerine (6). Stable angina is often the first symptom of an underlying CAD. Individual prognosis of stable angina differs depending on clinical characteristics and prevalence of risk factors (7).

ACS is the acute clinical manifestation of CAD (5). There are two known mechanisms behind ACS: plaque rupture and plaque erosion (5). Plaque rupture is appreciated to be the most common cause of coronary thrombosis. During this process, the fibrous cap that separates the lipid-rich- and necrotic core of an atherosclerotic plaque from the lumen of the artery ruptures, leading to thrombus formation. During thrombus formation, circulating platelets are activated by exposed subendothelial collagen, leading to a coagulation cascade that results in blood clot formation (8). Plaque erosion is a smaller lesion that only consists in the disruption of the endothelial layer, which also can lead to thrombosis and ACS (5).

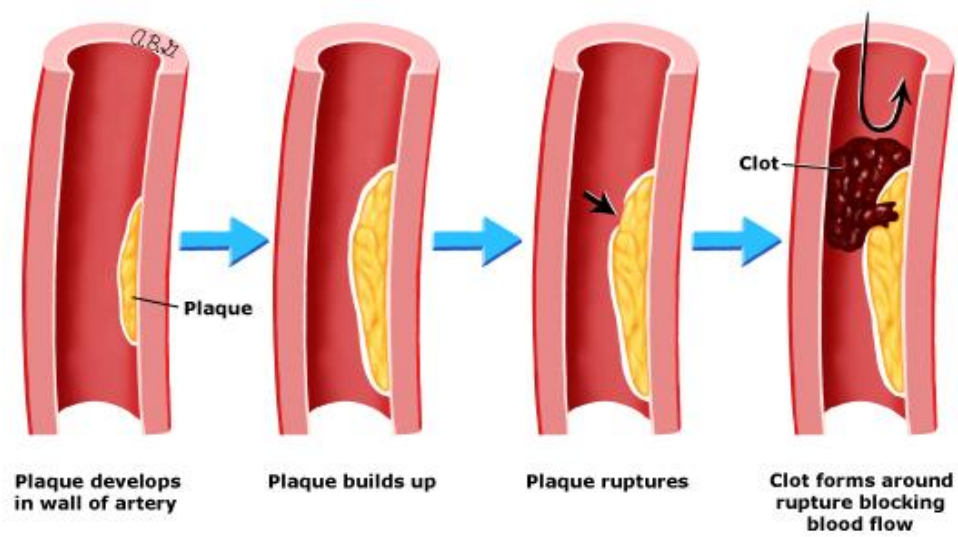

Figure 2. Artherosclerotic plaque progression

A schemitic drawing showing progression of an artehrosclerotic lesion. Reproduced with permission from: Aroesty JM. Patient education: Stenting for the heart (Beyond the Basics) In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on [2020/12/11].) Copyright © 2020 UpToDate, Inc. For more information visit www.uptodate.com.

The clinical manifestations of ACS are unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI). UA and NSTEMI are related conditions, both characterized by symptoms suggestive of acute ischaemia (e.g., chest pain with or without dyspnoea, radiation of pain to arms, jaws, neck or back, and nausea), occurring de novo or increasing in frequency, duration and/or intensity over time, with or without ST-segment depression on the electrocardiogram (ECG). The distinction between UA and NSTEMI is made by the absence or presence of circulating biomarkers of myocardial necrosis, respectively. STEMI is a clinical condition characterised by symptoms indicating acute ischaemia together with ST-segment elevation on the ECG, indicating an MI with transmural ischaemia (9, 10).

During an MI, blood-flow to a part of the myocardium is decreased or cut-off (Figure 2). The size and severity of the MI depends on whether the artery is partially or completely obstructed, on the location of the thrombus, as well as on the presence and extent of collateral circulation (9). An entirely occluding thrombus typically leads to STEMI. Partial occlusion, or occlusion in the presence of collateral circulation, results in NSTEMI or UA (10). The limited blood-flow leads to ischemia which in turn can lead to necrosis and loss of function of the cardiomyocytes.

Epidemiology of cardiovascular disease

CVD is the most common cause of death globally (2), causing approximately 30% of all deaths; 85% of which are due to MI or stroke (1). More than 4 million people die from CVD across Europe every year, with 1.4 million of these deaths occurring before the age of 75 (11).

In 2015, there were >85 million people in Europe living with CVD (12). The main reasons for this high prevalence are considered to be an aging population, unhealthy diet, smoking, sedentary lifestyles, increasing obesity, and DM (13).

In Sweden, the incidence of ACS has decreased in recent years as reported by the Public Health Agency (14). The main reasons for this are believed to be a decrease in smoking rates and better medical treatments for hypertension and dyslipidaemia (15). However, a recent Swedish population-based study demonstrated that the decrease in deaths due to CVD was mostly attributable to changes in risk factors in the general population and to a lesser extent cardioprotective medication emphasizing the importance of public health measures as a part of primary prevention (16).

Decrease in mortality from cardiovascular disease

Mortality from CVD has decreased in the last decade. However, epidemiological studies show wide differences across Europe in CVD mortality, with large differences in death rates across countries and with a small number of countries still experiencing an increase (11, 17).

Risk factors for cardiovascular disease

Developing CVD is linked to several risk factors (18). A risk factor is an attribute that increases the likelihood for an individual to develop disease and is causal to disease development. Causality can be predicted with observational and interventional studies (19). For CVD, the risk factors are defined as being either modifiable or non-modifiable. Their direct causality has been established to a varying degree, as discussed below (2). Because of established causality, risk factors can be used to predict CVD using scoring systems (20).

Non-modifiable risk factors

Non-modifiable risk factors include age, gender, family history, race, and ethnicity (18, 21-23).

Age

Older age is associated with greater risk for CVD and age is an independent risk factor for developing CVD (21). However, when age and other risk factors are used together to estimate future CVD risk, it has been established that the contribution of age in multivariable models may reflect the intensity and duration of exposure to other risk factors (24). Thus, the age-associated risk of CVD can be minimized by modification of traditional modifiable-risk factors.

Gender

It has been observed that females have a later onset of CVD, higher mortality rates and a worse prognosis from CVD than males due to differences in anatomy and hormone-related protection and due to differences in clinical presentation (23). For instance, menopause is associated with a significantly increased CVD risk. The increased risk is believed to be due to the negative effects of oestrogen withdrawal that effects several CVD risk factors including changes in body fat distribution, reduced glucose tolerance, dyslipidaemia, hypertension, increased sympathetic tone, endothelial dysfunction and vascular inflammation (25). However, it has been theorized that gender is more of a social determinant of CVD, meaning that gender shapes adoption of health behaviours, making gender a modifiable determinant of CVD through efforts of improving gender equality (22). However, more research is needed to establish this.

Family history

Family history of premature CVD in a first-degree relative increases the risk of CVD. Family history is not a part of CVD risk scoring systems used in clinical practice today (18). However, genetic studies show great potential in identifying individuals at increased CVD risk. Studies on polygenetic risk scores associated with CAD identifying patients with "high genetic risk" have demonstrated that these patients greatly benefitted from both a healthy lifestyle (defined as not smoking, not being obese, being physically active at least once weekly, and having a healthy diet), as well as lipid-lowering medication to prevent a first coronary event (26, 27).

Ethnicity

CVD variations exist for groups of different ethnic backgrounds living in the Western world. For example, in the United States of America (USA) rates of ACS in the African American community have been higher than those in other races, with the incidence in black women outpacing that in white men. Studies have shown that some minority groups in the USA have higher rates of traditional CVD risk factors, different rates of treatment with revascularization procedures, and excess morbidity and mortality from CVD (28, 29). Thus, to some extent it could, like gender, be modifiable though social equality.

Modifiable risk factors

Modifiable risk factors are behaviours and exposures that can increase or decrease the risk of CVD.

In 2004 the INTERHEART study, a world-wide case-control study of patients with acute MI, suggested that dyslipidaemia, smoking, hypertension, DM, abdominal obesity, psychosocial factors, low consumption of fruits and vegetables, and increased consumption of alcohol, as well as lack of regular physical activity accounted for most of the risk of MI for both men and women, irrespective of age or geography (30).

The Framingham study, a population-based observational study, has also been in the frontline in identifying and analysing modifiable risk factors for CVD. The Framingham study group recognised that CVD risk factors are multifactorial and interact over time (20, 31).

Dyslipidaemia

Dyslipidaemia refers to abnormal levels of blood lipids (mainly LDL-cholesterol, high-density lipoprotein (HDL)-cholesterol and triglycerides). Evidence suggests that LDL-cholesterol is both the cause and the driving force of atherosclerosis (2, 4, 12). Numerous studies have consistently demonstrated a log-linear relationship between the levels of plasma LDL-cholesterol and the risk of CVD (4, 12). It appears that the effect of LDL-cholesterol on CVD risk can be predicted by both the magnitude and duration of exposure. Studies on lipid lowering medication have found that lowering the LDL-cholesterol levels is associated with significantly lower CVD risk with no clear lower limit for achieved LDL-cholesterol values (12, 32).

The INTERHEART study demonstrated that dyslipidaemia was the most common risk factor preceding an MI (30). Regarding the prevalence of dyslipidaemia, a recent European observational study on individuals ≥50 years of age with no prior history of CVD found that prevalence of dyslipidaemia was 20% and that the prevalence was higher in individuals who had DM or increased CVD risk for other reasons (33).

Smoking

Tobacco smoking negatively affects vascular biology, though its mechanisms are not fully understood (2, 34). Smoking enhances the development of both atherosclerosis and thrombi formation by affecting endothelial function, oxidative processes, platelet function, fibrinolysis, inflammation, lipid oxidation and vasomotor function (18, 34). Tobacco smokers are more likely to develop various forms of cancer, DM, as wells as cardiovascular, and respiratory diseases (35). Epidemiologic studies strongly support the assertion that tobacco smoking increases the incidence of CAD (34).

Tobacco smoking is a worldwide health and economic burden. As the World Health Organisation (WHO) states:

> **"**The tobacco epidemic is one of the biggest public health threats the world has ever faced, killing more than 8 million people a year around the world" (35)

In Sweden, tobacco smoking has decreased in the last decades. In the year 2018, only 7% of the population aged 16-74 smoked (36). However, like in the rest of the world, tobacco smoking is still one of the biggest risk factors for disease morbidity and mortality in general.

Hypertension

Hypertension is defined as the BP level at which the benefits of treatment (either with lifestyle interventions or drugs) outweigh the risks of treatment, as documented by clinical trials (37). Hypertension drives the atherosclerotic process forward by increasing arterial wall tension, disturbing repair processes, leading to endothelial dysfunction and aneurysm formation (3). Similar to LDL-cholesterol, studies have demonstrated that there is a proportional relationship between BP lowering and reduction in CVD morbidity and mortality (38). Treatment targets differ for different age groups and presence of other concomitant risk factors (37). However, a recent analysis pooling previous studies of hypertension suggested that, in the presence of CVD, lowering the BP is beneficial no matter the starting BP. The study demonstrated that over an average four years of follow-up time, a 5 mmHg decrease in systolic BP (SBP) reduced the relative risk of major cardiovascular events by 10% (39).

Globally, hypertension is a major cause of preventable CVD and all-cause death. Hypertension is common, with an overall prevalence in adults around 30 − 45%. (37).

Diabetes mellitus

DM is a disorder in which blood glucose levels are abnormally high due to insulin resistance or insufficient insulin production (40). Hyperglycaemia and insulin resistance lead to vascular atherosclerosis via multiple molecular pathways (41). Also, abdominal fatty tissue, often associated with insulin resistance and type 2 DM, contains inflammatory cells that secrete mediators of inflammation (2, 42). Biomarkers of inflammation, notably C-reactive protein (CRP), prospectively predict CVD risk and increase simultaneously to other CVD risk factors (2, 43).

There are several types of DM including, type 1 and type 2. Type 2 DM is the most common type, accounting for about 90% of all DM cases. In 2017, roughly 60 million adult Europeans were estimated to have type 2 DM (44). The global prevalence of DM is continuously increasing as more people adapt a Western lifestyle. The prevalence of DM in patients with CVD is high. In Sweden, the overall

prevalence of DM is around 5% (45), but for patients admitted to hospitals for ACS the prevalence is 24% (46). Also, in a study from 2002 Norhammar *et al.* demonstrated that oral glucose tolerance tests (OGTT) revealed that two-thirds of MI patients without known DM had newly detected DM or pre-DM (47). Current guidelines recommend screening of all CVD patients for DM (44).

Excess weight

Overweight and obesity are defined as excess fat mass that impairs health (48). It is most often measured by calculating the body mass index (BMI), which is an index of weight-for-height (49). Overweight is defined as BMI 25-30 kg/m^2 and obesity BMI ≥30 kg/m^2 (18, 48). As previously described for DM and insulin resistance the link to CVD to through abdominal body fat that secretes inflammatory mediators (2, 42). Excess weight also leads several other adverse effects, like changes in body composition that can affect hemodynamics and heart structure, increasing insulin resistance, increasing BP, and leading to dyslipidaemia (50, 51). Due to the clinically important role of abdominal body fat, waist circumference should also be measured (51). Both BMI and waist circumference have been shown to strongly predict the risk of CAD (49, 52). This is especially true for first time CAD, since several studies have reported a phenomenon called the obesity paradox where overweight and obese people with an established CAD have a better prognosis compared with the non-overweight or non-obese, the reasons for which are not clear (50, 51). However, some argue that the observed obesity paradox is due to selection bias (53).

Globally, the prevalence of overweight and obesity has increased in the last decades (50). According to WHO, in 2016, 39% of adults were overweight and roughly 13% were obese (48).

Diet

Dietary habits can affect the risk of developing CVD both indirectly, by affecting weight, BP, or blood-lipids, as well as more directly, by reducing oxidative stress with antioxidants, although the evidence behind this is not yet conclusive (18, 54). To lower CVD risk, the specific nutrients of interest are fatty acids (mainly affecting blood-lipid levels), minerals (mainly affecting BP), vitamins and fibre (18). In 2013, a Swedish prospective study evaluated diet quality, as measured by adherence to the 2005 Swedish dietary guidelines (low intake of saturated fat and sugar, and higher intake of dietary fibre, fish, fruits, and vegetables). The results showed that after a follow-up of 16 years participants with a high-quality diet had a lower risk of cardiovascular events (55).

There are multiple methods for studying dietary intake, often relying on self-assessment which has limitations discussed later on (56). A recent study, on the health effects of dietary patterns in 195 countries, demonstrated that consumption of nearly all healthy foods was suboptimal, with a generally low intake of nuts and

seeds, milk and whole grains and high intake of sugar-sweetened drinks, processed- and red meat (57).

Physical inactivity and sedentary lifestyle

The WHO defines physical activity as any bodily movement by skeletal muscles that requires energy expenditure (58). Physical inactivity is one of the major risk factors for CVD (18, 59). The mechanisms behind the effects of sedentary behaviour on cardiovascular health are multifactorial (51). The potential benefits of physical activity affect multiple risk factors, for example by reducing BP (60), reducing systemic inflammation (61), reducing visceral adiposity (62), and, improving insulin sensitivity (63). Regular physical activity reduces the risk of many adverse health outcomes in a dose–response fashion (64, 65).

Globally, roughly 25% of adults and over 80% of adolescents do not meet the recommended levels of physical activity and there has been no improvement in these numbers in the last 20 years (58).

Psychosocial factors

Psychosocial risk factors include low-education level, low-income, social isolation, exposure to stressors, depression, and anxiety (18, 66). They have individually or together been associated with increased risk for CVD. The relationship between psychosocial factors and CVD is complex, based on both biological factors and behavioural patterns (66-68).

Reporting the general prevalence of psychosocial risk factors is not done here since the risk factors are multiple and complex. It has, however, been observed that psychosocial risk factors seem to cluster in individuals and groups. For example, people of lower socioeconomic status are more likely to be depressed, and socially isolated (18, 69).

Cumulative effect of risk factors

Individually, dyslipidaemia and tobacco smoking are the most important risk factors for CVD. However, few individuals have only one isolated risk factor. The INTERHEART study made a model estimate of the effect of exposure to multiple risk factors. Figure 3 shows how the effect of multiple risk factors increased the risk of MI. Jointly, tobacco smoking, hypertension, and DM increased the odds ratio for acute MI to 13.0 compared to those without these risk factors, addition of dyslipidaemia (as indicated by apolipoproteins) increased the odds ratio to 42.3, and finally, addition of abdominal obesity further increased odds ratio to 68.5 (30).

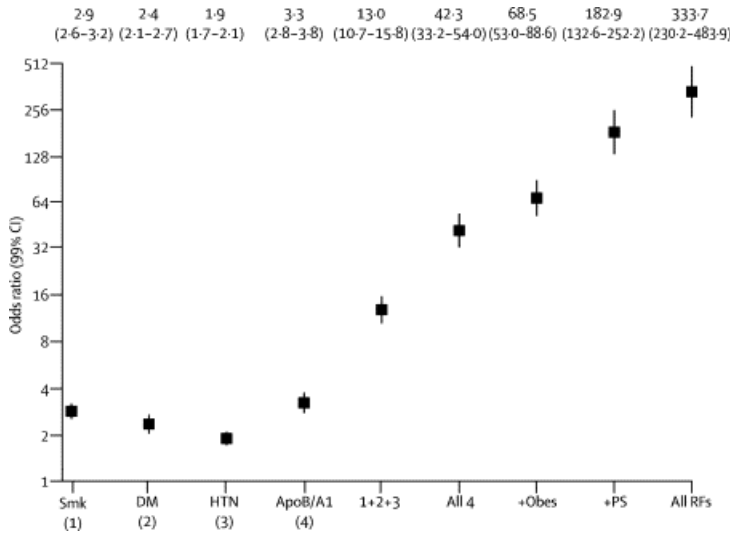

Figure 3. Risk of myocardial infarction associated with exposure to multiple risk factors

Note the doubling scale on the Y axis. The odds ratios are based on never smoking, top lowest tertile for abdominal obesity, and top lowest quintile for apolipoproteins. If these three are substituted by current and former smoking, top two tertiles for abdominal obesity and top four quintiles for apolipoproteins, then the odds ratio for the combined risk factor is 129.20. Smk=smoking, DM=diabetes mellitus, HTN=hypertension, ApoB/A1= apolipoprotein ratio: B/A1, Obes=obesity, PS=psychosocial, RF=risk factor. Reproduced with permission from Yusuf *et al* (30) © Elsevier.

Scoring systems

Many different scoring systems exist to estimate CVD risk in individuals based on their risk factor profile. Here are two examples.

- The Systematic Coronary Risk Estimation (SCORE) system is recommended by European guidelines to be used in primary prevention. It is used to estimate a person's 10-year risk of death due to CVD, considering gender, smoking status, age, SBP and total cholesterol (18).
- The Second manifestations of arterial disease (SMART) risk score was developed for use in individuals with an established CVD. It uses age, gender, smoking status, SBP, HDL-cholesterol, total cholesterol, estimated glomerular filtration rate (eGFR), CRP, prior medical history (CVD, DM and abdominal aortic aneurysm), as well as time since first diagnosis of CVD, to estimate the 10-year risk for MI, stroke, or vascular death (70, 71).

Initial treatment of acute coronary syndrome

Treatment of ACS has evolved a great deal in the last decades (9). In the acute setting, current guidelines recommend revascularization of the coronary arteries with percutaneous coronary intervention (PCI), or in some cases, coronary artery bypass grafting (CABG). PCI involves coronary catheterization via the femoral or radial artery and visualization the coronary arteries using X-ray and contrast material. Once a significant coronary artery stenosis or occlusion is located, the procedure involves balloon angioplasty to widen the lumen, and stent placement to maintain the integrity of the lumen. In case of PCI, the beneficial effect of reperfusion is greatest when performed as soon as possible. In some cases, for example in the case of a three-vessel disease, CABG is the treatment of choice. CABG is open thoracic surgery, where coronary arterial circulation is re-established using vessel grafting.

Medical treatment and lifestyle modifications should be initiated as soon as diagnosis is made (9, 18). The recommended pharmaceuticals have different roles in preventing new coronary events. Antiplatelet therapy with acetylsalicylic acid (ASA) and P_2Y_{12} inhibitors reduce the risk of recurrent thrombus formation (9). HMG-CoA reductase inhibitors (i.e., statins), a rate-limiting enzyme in the synthesis of cholesterol, have in multiple studies been shown to reduce CVD events due to their cholesterol-lowering effects (2, 32). BP-lowering drugs are, for example, angiotensin-converting enzyme inhibitors (ACEi) or angiotensin-II receptor blocker (ARB) and β-blockers (38). The effect of BP lowering drugs in reducing the risk of recurrent MI is largely due to the BP reduction, with one exception, an extra initial cardioprotective effect of β-blockers in people who have recently suffered and MI (38).

Prognosis after myocardial infarction

When patients have suffered an MI, they are defined as having an established CAD and are at high-risk for developing a new MI. A Swedish retrospective registry study from 2015 found that one year after suffering an MI, patients had an 18.3% risk of developing a new cardiovascular event (MI, stroke, or cardiovascular death) and that high-risk patients (with at least one of the following prior to index MI: DM, at least one MI prior, CABG, peripheral arterial disease, stroke, heart failure, or diagnosis of chronic renal dysfunction) had a higher cumulative probability of suffering a new event (Figure 4) (72).

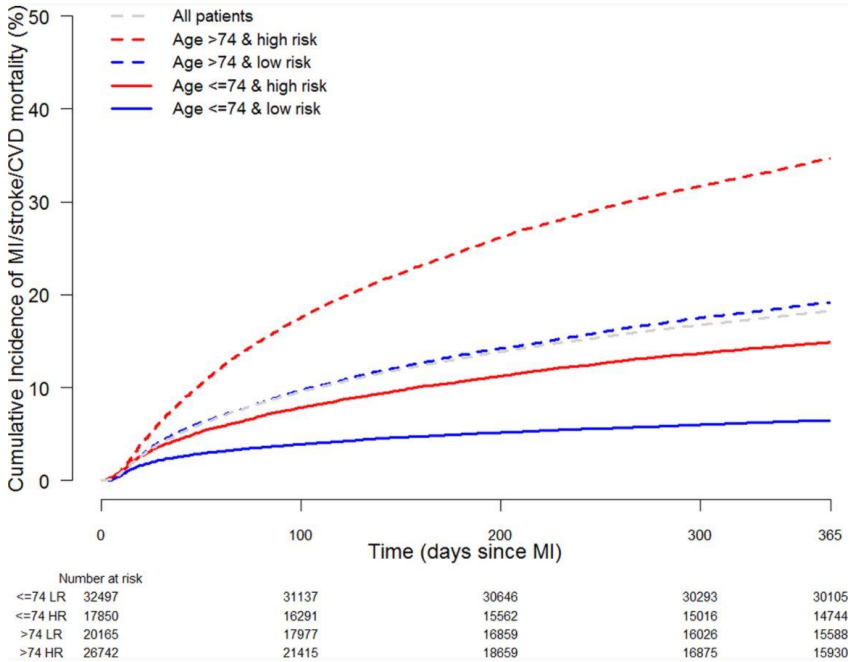

Figure 4. The risk for new cardiovascular event

A Kaplan-Meier estimate of the risk for a new cardiovascular event (MI, ischaemic stroke, or cardiovascular death) during the first 365 days after suffering an MI, stratified by age and high- and low-risk patients. The figure is reproduced with permission from Jernberg *et al* (72) © Oxford University Press.

Post-MI patients should be subjected to intense cardioprotective treatment to prevent future acute coronary events. After surviving a first coronary event, patients may enter a more stable phase of the disease called chronic coronary syndrome (CCS) (73). As the name indicates CAD is a chronic disease and patients are subjected to life-long therapy.

Prevention of cardiovascular disease

To prevent CVD, modifiable risk factors need to be addressed. Prevention is defined according to the absence or presence of an established CAD.

- **Primary prevention:** In the absence of an established CAD, the purpose of primary prevention is to prevent CAD from developing. This is done both on a population level as a part of public health interventions and on an individual level, addressing individual risk factors.
- **Secondary prevention:** In the presence of an established CAD, the purpose of secondary prevention is to manage the disease and prevent new coronary events. This is done on an individual level and delivered through, for example, cardiac rehabilitation programmes or primary care.

Cardiac rehabilitation

Comprehensive cardiac rehabilitation programmes are complex multidisciplinary interventions including patient assessment, management and control of cardiovascular risk factors, physical activity counselling, prescription of exercise training, dietary advice, psychosocial management, and vocational support (18, 74, 75). The primary goal of cardiac rehabilitation is to reduce risk factor burden in patients that have an established CAD and to improve long-term prognosis. Reducing risk factor burden has been shown to be the most effective way to prevent recurring cardiovascular events (17, 75-77).

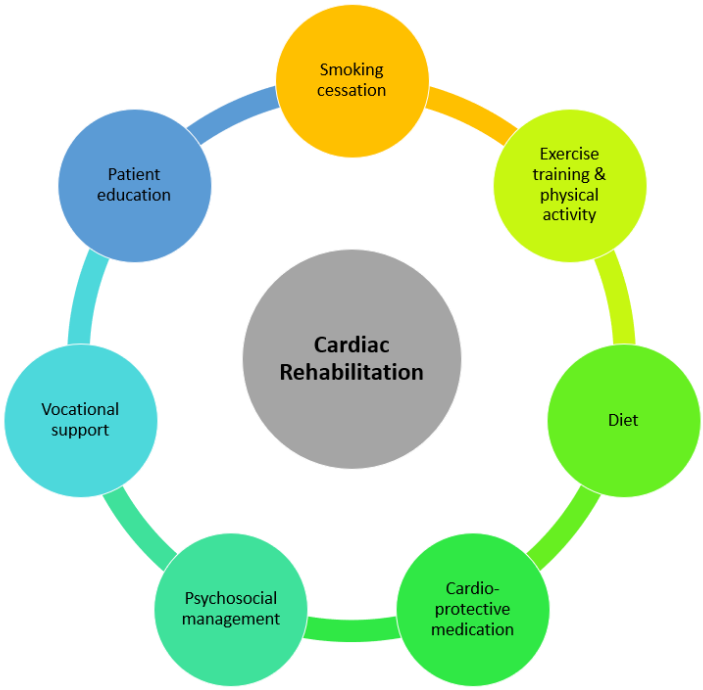

Figure 5. Principal components of cardiac rehabilitation.
Outline of the principal components of comprehensive cardiac rehabilitation programmes.

History of cardiac rehabilitation

Cardiac rehabilitation has changed dramatically since the early 1900s (78). During that time patients were restricted to many weeks of bed rest after suffering an MI, often leading to deconditioning, decline in functional capacity, prolonged hospital stays, as well as increased morbidity and mortality. In the 1940s, the chair therapy was introduced where patients got out of their chairs and walked around the hospital wards. This was the first of many changes focusing on increased physical activity. Since then, both the acute and long-term care after MI has changed dramatically with new interventions and medications (79, 80).

In Sweden, the first cardiac rehabilitation centre was started in 1987 at Skåne University hospital in Malmö by local nurses (81). Other hospitals and primary care centres subsequently followed the example starting up structured secondary prevention for post-MI patients (82). Today there are approximately 80 cardiac rehabilitation centres in Sweden (83).

In 2016, The Cardiac Rehabilitation Outcome Study (CROS) was the first meta-analysis evaluating the effect of structured multi-component cardiac rehabilitation in the era of modern cardiology including statin-therapy, PCI, and CABG. It

confirmed a beneficial effect of cardiac rehabilitation on total mortality after MI (76).

In 2020, the importance of quality of cardiac rehabilitation and the need of meeting minimal requirements has been addressed in the follow-up study: CROS-II (84). The study confirmed that cardiac rehabilitation is effective in reducing total mortality when delivered to certain pre-specified standards, including an individually fitted and supervised exercise training programme and a comprehensible treatment of all cardiovascular risk factors.

Cardiac rehabilitation today

Cardiac rehabilitation has a strong evidence base. In the European Guidelines of Cardiovascular Disease Prevention cardiac rehabilitation after MI is given a Class I, Level A recommendation (18). A Class I recommendation means that there is evidence that the given procedure is beneficial, useful, and effective. Levels refer to the level of evidence and for Level A data is derived from multiple randomized controlled trials (RCT) and/or meta-analyses (18). The IA recommendation is the highest form of recommendation. The European guidelines form the structure and content of cardiac rehabilitation in Sweden.

Structure of cardiac rehabilitation

European recommendations on the duration and structure of cardiac rehabilitation programmes were published in 2014 (74), updated in 2020 (75), and are summarised in Figure 6. In short, cardiac rehabilitation should be delivered by a multidisciplinary team of healthcare professionals, including a programme coordinator (cardiologist), nurses and exercise experts, and led by a medical director. The programme should be introduced in-hospital and start at the latest 3 weeks post discharge. It should last for a minimum of 8 weeks, but preferably for 1 year. The cardiac rehabilitation programme should have a clear organisation, with leadership, regular meetings, and regular audits.

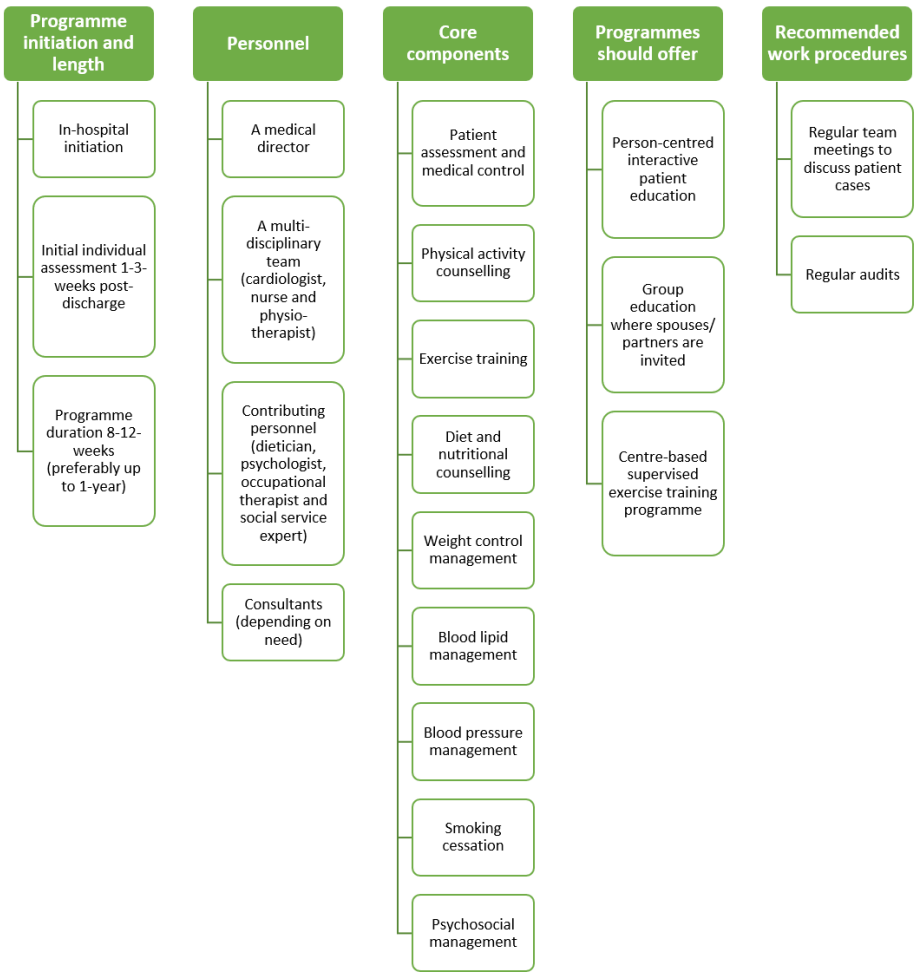

Figure 6. The core components of cardiac rehabilitation
A flow-chart demonstrating ther core components of cardiac rehabilitation accoring to European Guidelines (74, 75).

Cardiac rehabilitation is, traditionally, divided into 3 phases (74, 75, 78).

- **Phase I** is initiated in-hospital. It consists of early mobilization of the cardiac patient, introducing cardioprotective medication and lifestyle advise. The shorter hospital stay with modern cardiology gives a limited time for conducting a comprehensive in-hospital cardiac rehabilitation programme. However, the programmes should be initiated in-hospital laying the ground for the next phase.
- **Phase II** may be provided in-hospital or in an outpatient setting. It is a supervised programme, delivering the core components (Figure 6) aiming

for clinical stabilization, risk factor control and promotion of long-term CVD prevention through lifestyle modification.

- **Phase III** is a lifetime maintenance phase with continued focus on maintaining a healthy lifestyle and continued risk factor control. The goal is for patients to have access to long-term services maintaining the preventive and rehabilitative work done in phase II.

Content and therapeutic goals of cardiac rehabilitation

In Sweden, secondary preventive therapeutic goals are derived from the European guidelines of Cardiovascular disease prevention (18) (Table 1).

Patients that participate in cardiac rehabilitation are, routinely, already prescribed cardioprotective medication initiated during their hospital stay. During the cardiac rehabilitation programme, the medical treatment is optimised by dose adjustment and/or adding or removing medication. Programmes should also include medical management of DM.

Lifestyle changes are an important part of risk reduction; they include exercise training and increased physical activity, healthy diet, smoking cessation, as well as promotion of psychosocial health and stress management.

Smoking cessation should by aided by any means necessary. Giving up smoking is associated with a considerable reduction in risk of all-cause mortality among patients with CAD (77, 85). There is a strong evidence base for brief interventions including advice to give up smoking, nicotine replacement therapy, and medication such as bupropion and varenicline (18).

At the start of a comprehensive cardiac rehabilitation programme, patients are encouraged to participate in exercise-based cardiac rehabilitation (exCR) led by physiotherapists. ExCR includes individually prescribed, supervised exercise training and physical activity counselling (74, 86). Exercise training and physical activity have a strong foundation within cardiac rehabilitation (87). ExCR reduces the risk of cardiovascular mortality and the risk of hospitalisation, and regular physical activity reduces the risk of all-cause and CVD mortality (64, 65).

Table 1. Goals for risk factor control in cardiac rehabilitation according to European guidelines (12, 18, 37, 75, 86).

Secondary preventive therapeutic goals	
Smoking	No exposure to tobacco in any form.
Blood pressure	<130/80 mmHg, if tolerated, but not <120/70. Age ≥65 SBP taget range is 130-140.*
LDL cholesterol	<1.4 mmol/L and a reduction of at least 50%**.
Physical activity	Moderate aerobic physical activity for ≥150 minutes/week or vigorous aerobic physical activity ≥75 minutes/week.
Exercise training	Participation in exCR. Individually tailored exercise recommendations.
Diet	Saturated fatty acids to account for <10% of total energy intake, through replacement by polyunsaturated fatty acids. Trans unsaturated fatty acids: as little as possible. <5 g of salt/day. 30–45 g of fibre/day, preferably from wholegrain products. 200 g of fruit/day (2–3 servings). 200 g of vegetables/day (2–3 servings). Fish 1–2 times/week, one of which is to be oily. 30 g of unsalted nuts per day. Sugar-sweetened soft drinks are discouraged. Alcoholic beverages are discouraged. If consumed, consumption of alcoholic beverages should be limited to two glasses/day for men and one glass per day for women.
Body weight	BMI 20-25 kg/m2, waist circumference <94 cm for men and <80cm for women.
Diabetes mellitus	HbA1c <7% (<53 mmol/mol), preferably <48 mmol/mol.

SBP, systolic blood pressure; LDL, low-density lipoprotein; exCR, exercise-based cardiac rehabilitation; BMI, body mass index; HbA1c, Haemoglobin A1c. *The target level of BP changed in the most recent European guidelines from <140/90 mmHg to <130/80 mmHg. The <140/90 mmHg goal is used in the studies included in this thesis (37). **The target level of LDL-cholesterol changed in the most recet European guidelines from <1.8 mmol/L to <1.4 mmol/L. The <1.8 mmol/L therapeutic goal is used in the studies included in this thesis (12).

Following a diet rich in healthy oils and plant-based food has been shown to reduce cardiovascular events (30, 88, 89). Based on current evidence, a Mediterranean-style diet is recommended. In 2001 the Lyon Diet Heart Study was published. It was an RCT in a secondary preventive setting that tested the effectiveness of a Mediterranean diet. The study was stopped early because of significant beneficial effects of the Mediterranean diet with a 50-70% lower risk of recurrent heart disease (cardiac death, nonfatal MI, UA, stroke, heart failure, and pulmonary or peripheral embolism) in the group randomized to the Mediterranean diet (89). In 2018 the Prevención con Dieta Mediterránea (PREDIMED) trial was published, also an RCT. It compared the effects of two Mediterranean-style diets, one with added olive oil and one with added nuts, with a reduced fat diet, in patients at high CVD risk. The trial resulted in a decrease in cardiovascular events in participants assigned to the diet with added olive oil or nuts (88). However, a recent meta-analysis on the effects of the Mediterranean diet in secondary prevention resulted in some uncertainty regarding the effects on clinical endpoints and cardiovascular disease risk factors (90). It should be kept in mind that studies on diet in relation to disease have

methodological problems, since diet is not a single exposure but rather a complex set of interconnected variables (56, 91).

Psychosocial health should also be addressed during cardiac rehabilitation. Studies on depression and anxiety and CVD have displayed an association with worse cardiac outcomes and mortality (92, 93). One possible reason for this might be the lack of medication adherence (94). Regarding management, current guidelines recommend psychotherapy and/or antidepressants or anxiolytics (18). Psychosocial health also involves stress management. Previous studies have shown positive effects of stress management on the recurrence of cardiac events or cardiac death. However, according to a Cochrane review, the quality of evidence is still low grade (95, 96).

Vocational support involves interventions to help individuals overcome barriers to continuing with work (74). Vocational support and psychosocial management go hand in hand since vocational reintegration after MI is largely determined by psychosocial parameters, and to a lesser extent by the underlying cardiac condition (97).

Cognitive behavioural methods to facilitate lifestyle changes are given a IA recommendation in current guidelines (18). These include motivational interviewing aiming to support the patients in adopting a new and healthy lifestyle by identifying and mobilising one's own values and goals to stimulate behavioural changes (98).

Patient education should be provided. Education should include information on the purpose of the cardiac rehabilitation programme and the importance of each programme component (74). Swedish cardiac rehabilitation centres commonly offer participation in interactive group education called Heart School. A recent Swedish study on attending Heart School and long-term outcome (2-year and 5-year) after MI showed that attenders had a lower risk for both all-cause mortality and cardiovascular mortality (99).

Uptake, adherence, and outcomes of cardiac rehabilitation

Uptake and adherence to cardiac rehabilitation

Despite the known benefits of cardiac rehabilitation, programme uptake and patient adherence are suboptimal, for reasons that are complex and only partially understood.

Since 1995, the European Action on Secondary and Primary Prevention by Intervention to Reduce Events (EUROASPIRE) surveys have, through multinational inventories, sought to track lifestyle, risk factor control, and use of cardiac rehabilitation programmes in Europe (100-103). The latest survey,

published in 2019, showed that only 46% of patients were advised to participate in a cardiac rehabilitation programme after a coronary event and 69% of those advised attended at least one-half of programme sessions. The results indicate that cardiac rehabilitation seems to be greatly underutilised in Europe, largely due to lack of referral (103).

Attendance in cardiac rehabilitation in Sweden is described in the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry. The registry data shows more favourable attendance rates compared to EUROASPIRE, with 80% of all post-MI patients <80 years attending cardiac rehabilitation (83). Reasons for the better attendance rate compared to the rest of Europe may in part be the automatic referral system within the SWEDEHEART registry.

Barriers for participation in cardiac rehabilitation programmes may be related to patient's perception of illness. In 2015, Perk *et al* published an observational study on outcome of patient education after PCI (104). The study showed that 67% of post-MI patients believed they were cured after their PCI and only 38%, after receiving patient education, identified a need to change their lifestyle habits, mainly attributing their disease to non-modifiable risk factors.

Reasons may also be partially explained by patient traits and societal issues, with certain groups being underrepresented in cardiac rehabilitation programmes. A recent meta-analysis showed that females, older individuals, unemployed, people of low-income and people with increased comorbidity had lower participation rates (105). In Sweden, however, participation of males and females has been equal for some years (106, 107).

Lower participation in cardiac rehabilitation has also been seen with an increased geographical distance to cardiac rehabilitation centres (105, 107).

Patient outcomes after cardiac rehabilitation

The EUROASPIRE surveys (I-V) have observed large deficiencies in risk factor control after MI (101-103). In the latest survey (EUROASPIRE V) a total of 8261 patients who had suffered an MI or undergone PCI, or CABG were interviewed and examined approximately 6 months post-event (103). The results showed that 55% of smokers were persistent smokers, 38% were obese, 42% had BP ≥149/90 mmHg, 71% had LDL cholesterol ≥1.8 mmol/L, and 66% were not physically active for at least 30 minutes and 5 times/week. This shows that most patients do not reach their secondary preventive therapeutic goals. Furthermore, findings consistently display that the attainment of therapeutic goals varies considerably between different cardiac rehabilitation centres and countries (108-110).

The same trends have been demonstrated on risk factor control after MI in other international surveys and in Sweden (111). The SWEDEHEART 2019 annual report

demonstrated that, similarly to the EUROASPIRE V results, about half of the smokers remain persistent smokers after one-year post-MI, and just 19% took part in a 3-month long exCR programme. However, a larger proportion had attained the therapeutic goal for BP and LDL-cholesterol when compared to EUROASPIRE V (83). Similar to EUROASPIRE, the SWEDEHEART annual report also revealed a substantial variation in therapeutic goal attainment between different cardiac rehabilitation centres (83).

Modes of delivery of cardiac rehabilitation

To improve participation in cardiac rehabilitation and patient outcomes multiple studies on modes of delivering cardiac rehabilitation have been published.

A systematic analysis from 2019 found that some methods to increase enrolment in cardiac rehabilitation were effective, particularly those that targeted healthcare providers, such as training nurses or allied healthcare professionals (e.g., physiotherapists) and included a face-to-face programme delivery format (112).

Several studies have demonstrated that cardiac rehabilitation programmes coordinated by nurses can improve lifestyle, risk factor control and quality of life (113, 114).

There is also evidence that a long-term programmes focusing on behavioural changes and patient education can be effective in reducing cardiovascular events as well as improving lifestyle habits (115, 116).

eHealth

eHealth is a term for using digital technology in healthcare. International health organisations have put focus on the development of eHealth, hoping that it may increase adherence and accessibility to cardiac rehabilitation and to healthcare in general (75, 117, 118).

eHealth is a wide term for different modes of delivery of home-based healthcare including telephone support and text messages, smartphone applications, micro-letter applications, or remote monitoring, web-based or delivered via smartphone (mobile health or mHealth) (118).

The field of eHealth is new, and studies are being published at an increasing rate. The first systemic review on the effectiveness of mHealth and eHealth in cardiac rehabilitation was published in 2019. It concluded that mHealth and eHealth can improve secondary prevention of CAD, however, it highlighted heterogenicity in forms of delivery and outcomes being studied. The review called for more trials (119).

Current evidence

What is clear from previous studies is that for cardiac rehabilitation to work effectively it needs to be comprehensive and include the above-mentioned core components (Figure 6) (84). Also, the need for individually tailored therapeutic goals for different patient groups has recently been underlined (75). The European Society of Cardiology (ESC) has published a position paper on cardiac rehabilitation programmes presenting individually tailored core components presented for patients with different backgrounds and comorbidities (75).

Gaps in evidence

The 2016 European Guidelines on Cardiovascular Disease Prevention highlighted several gaps in evidence concerning cardiac rehabilitation, including the two following (18):

> "The optimal cardiac rehabilitation programme in the era of modern cardiology and the incremental benefits of various components of cardiac rehabilitation programmes, especially for underserved patient groups."

> "Alternative and cost-effective models of cardiac rehabilitation are needed to ensure participation globally, including low- and middle-income countries."

Summary and thesis purpose

CVD is a common disease caused largely by a set of modifiable risk factors. CVD is a chronic disease that is manifested acutely as ACS, after which patients are at high risk for recurrent coronary events. After the initial treatment of ACS, patients should receive secondary preventive therapy delivered though cardiac rehabilitation. The primary goal of cardiac rehabilitation is to treat modifiable risk factors with medication and lifestyle changes. While participation in comprehensive cardiac rehabilitation is the most effective way to prevent recurrent coronary events, uptake, adherence, and patient attainment of therapeutic goals is suboptimal.

There is a lack of knowledge on how to best ensure patient participation, motivate patients to programme adherence and lifestyle changes, and ensure programme accessibility.

The studies in this thesis aim to improve secondary preventive care for patients who have suffered an MI. First, we wanted to evaluate potential benefits of tailoring follow-up structure within cardiac rehabilitation to patient needs. Second, to perform an inventory of services provided within cardiac rehabilitation programmes across Sweden. Third, to evaluate whether the use of eHealth can improve patient´s

attainment of therapeutic goals in cardiac rehabilitation. Finally, to identify predictors of patient´s attainment of therapeutic goals within cardiac rehabilitation programmes.

Overview of papers

Table 2. An overview of papers included in this thesis

	Paper I	Paper II	Paper III	Paper IV
Design	Retrospective observational study.	Survey-based study.	Randomized controlled trial.	Observational registry and survey-based study.
Population	Patients (<75 years) who suffered an MI and took part in cardiac rehabilitation.	All Swedish cardiac rehabilitation centres.	Patients (<75 years) who suffered an MI and took part in cardiac rehabilitation.	Patients (<75 years) who suffered an MI and took part in cardiac rahabilitation.
Ethical consent	Yes (Dnr 2016/494)	Yes (Dnr:2336-001)	Yes (Dnr: 2016/5)	Yes (Dnr:2336-001)
Included (n)	n=217	n=79	n=150	n=9165
Study period	November 2013 to January 2016	Year 2016	Patient inclusion: April 2016 - April 2018. Follow-up completion in June 2019.	November 2015 to October 2016
Setting	Outpatient. Single centre. Sweden.	Multicentre. Sweden.	Outpatient. Multicentre. Sweden.	Outpatient. Multicentre. Sweden.
Database	SWEDEHEART.	Perfect-CR.	SWEDEHEART.	Perfect-CR, SWEDEHEART, Statistics Sweden.
Statistical methods	Regression analysis	Descriptive statistics.	Independent samples-t-test and regression analysis	Orthogonal partial least squares discriminant analysis.
Primary outcome	Comparative delta values for risk factors between baseline and follow-up (SBP, DBP, BMI, LDL, HDL, total cholesterol and triglycerides).	Programme characteristics of cardiac rehabilitation programmes.	Comparative delta values between two consequtive submaximal exercise tests.	Reaching LDL-cholesterol of <1.8 mmol/L, BP of <140/90 mmHg and smoking cessation (yes/no).

MI, myocardial infarction; Dnr, diarienummer (Registration number); n, number; SBP, systolic blood pressure, DBP; diastolic blood pressure; BMI, body mass index, LDL, low-denisty lipoprotein; HDL, high-density lipoprotein; BP, blood pressure.

Aims

Paper I

The aim of this study was to compare attainment of secondary preventive therapeutic goals after MI in patients attending individually tailored, nurse-led cardiac rehabilitation and patients attending traditional cardiac rehabilitation. The hypothesis was that patients receiving tailored cardiac rehabilitation would achieve secondary preventive therapeutic goals to a larger extent.

Paper II

The aim of this study was to evaluate the cardiac rehabilitation programme characteristics and programme adherence to European Guidelines on Cardiovascular Disease Prevention across all cardiac rehabilitation centres in Sweden.

Paper III

The aim of this study was to assess the effect of a web-based mobile-device application designed to support adherence to lifestyle advice and control of risk factors, as a complement to traditional cardiac rehabilitation, compared to receiving traditional cardiac rehabilitation alone. The hypothesis was that the web-based application would improve patients' adherence to lifestyle advice.

Paper IV

The aim of this study was to identify organizational and patient-level predictors for attaining secondary preventive therapeutic goals for LDL-cholesterol, BP, and smoking cessation one-year after MI, in a nationwide cohort of post-MI patients who participated in cardiac rehabilitation. The hypothesis was that certain

organizational and patient-level predictors might be identified as more meaningful than others for the likelihood of patients attaining therapeutic goals.

Methods

The work presented in this thesis has been based at the Cardiology Clinic of Skåne University Hospital in Malmö, Sweden.

Data sources

SWEDEHEART

Papers I-IV are all linked to the SWEDEHEART registry.

The SWEDEHEART registry started in 2009 through the merging of four quality registers (RIKS-HIA, SEPHIA, SCAAR, and the Swedish Cardiac Surgery Register) forming Sweden's largest quality registry (120, 121). The SWEDEHEART registry is currently composed of six sub-registries. Two of SWEDEHEARTs sub-registries have been used is this thesis. The first, RIKS-HIA, is the Swedish Hearts Intensive Care Admissions registry that collects data on MI patients while in-hospital, in the acute setting. RIKS-HIA was started in 1991 in Linköping in collaboration with surrounding hospitals. The register became a national quality registry in 1995. The second, SEPHIA, is SWEDEHERTs secondary prevention sub-registry. It collects data during the first year post-MI in the outpatient setting. SEPHIA was started in 2005, and at the time of this thesis, all cardiac rehabilitation centres reporting to RIKS HIA also reported to the SEPHIA registry.

Control of data quality within the SWEDEHEART registry is performed regularly and has shown a 90-95% coherence with hospital records (83).

The primary purpose of SWEDEHEART is to support development of evidence-based therapy in acute and chronic CAD, to provide hospitals and clinics with the opportunity for own quality control and to form a basis for research in the field of cardiology. The long-term goal is to contribute to a reduction in mortality and morbidity in patients and to increase the cost-effectiveness of care (120).

Patient information and consent

Each facility that registers data in SWEDEHEART has a responsibility to inform patients about registration. The patients are informed verbally about the registry and their right to have their information removed at any time (120).

The Perfect-CR study

The Perfect Cardiac Rehabilitation (Perfect-CR) study was an inventory on services provided at Swedish cardiac rehabilitation centres. It forms the basis for the studies presented in **Paper II** and **Paper IV**. The reason for initiating the study was that the mode of delivering cardiac rehabilitation has been shown to affect patient outcomes (84, 122, 123) and that patients outcomes vary between cardiac rehabilitation centres in Sweden (83). The study was inspired by previous national audits (124-126).

Planning started in 2015 by putting together a research team (cardiologists, physiotherapists and cardiac rehabilitation nurses) to design a questionnaire aiming to assess work routines and services at cardiac rehabilitation centres. The questionnaire was ready in the fall of 2016 and set up in a web-based survey system (Survey Monkey ®, SurveyMonkey Inc., San Mateo, California, USA, www.surveymonkey.com).

The questionnaire

The questionnaire included 120 questions (Supplementary material 1). It was composed mostly of multiple-choice questions with a fixed list of answers, for some multiple-choice questions it was possible to provide one answer and for some it was possible to provide one or more answers. Some questions provided the possibility for respondent to give free-text answers if none of the provided answers were applicable. There were also grading scales that provided statements where respondents were asked to agree or disagree on a scale on the range from one (disagree) to six (agree).

The questionnaire was not validated (127) but, before the study started, it was tested on a small number of cardiac rehabilitation centres followed by an assessment and amendment by the research team.

The questionnaire was sent out in November 2016 to all 79 cardiac rehabilitation centres which at the time reported to SWEDEHEART (Figure 7). There were no exclusion criteria, however, one centre closed its operation only weeks after the questionnaire was sent out and was excluded from analyses in Papers II and IV.

Statistics Sweden

Statistics Sweden is responsible for Swedish official statistics including the total population registry (128, 129). Statistics Sweden provided patient-level variables for the study presented in **Paper IV**. The statistics produced by Statistics Sweden are largely based on information submitted in various surveys.

Study populations, periods, and settings

Sweden has a publicly financed tax-based healthcare system, which includes coverage of both in-hospital and outpatient care as well as subsidies for medication. The patient co-finances a small part of the healthcare costs, and subsidies for medication increase with a maximum threshold for full coverage.

Each Swedish citizen has a unique personal identity number which is used for identification in healthcare and registries. This provides an opportunity to merge and cross-link registry and healthcare journal information for scientific purposes.

Paper I

The study was initially designed as an observational retrospective assessment of non-inferiority comparing follow-up routines. During a 14-month period, between 2013 to 2015, all patients (n=217) that were admitted due to MI to the coronary care unit at Skåne University Hospital in Malmö, Sweden, and registered in the SWEDEHEART registry were included in the study. The first patient was discharged from the coronary care unit in November 2013 and the last outpatient follow-up was completed in January 2016. During the time of the study, the SWEDEHEART registry had an age limit of 75 years, making this the cut-off age for our study (120). There were no other exclusion criteria. The patients were included in the local cardiac rehabilitation programme which changed from traditional to tailored, nurse-led care during the study period. The study group was, thus, divided by timeline. The first group of patients (n=105) received traditional care, and the latter group (n=112) received tailored, nurse-led care. The programme characteristics for traditional and tailored, nurse-led care are displayed in Table 3.

Table 3. Programme chracteristics of both traditional care and tailored, nurse-led care.

Setting	Time-point	Traditional care	Tailored, nurse-led care
In-hospital	Index event*	Collection of registry data (RIKS HIA).	Collection of registry data (RIKS HIA). Patient received standardized information about the cardiac rehabilitation follow-up as a part of the discharge protocol.
Out-patient	6-10 weeks*	Follow-up visit with a nurse and first registry visit (SEPHIA).	Follow-up visit with a nurse and first registry visit (SEPHIA). Assessment of the need for a cardiologist consultation.
	3 months	Cardiologist consultation and referral to primary care.	Cardiologist consultation for patients with remaining significant coronary stenosis, ejection fraction <35%, remaining symptoms, or having undergone CABG.
	6-8 months		Patient received a standardized letter promoting a healthy lifestyle. Blood tests were taken and followed-up by telefone if needed.
	12-14 months*	Follow-up visit with a nurse and second registry visit (SEPHIA).	Follow-up visit with a nurse and second registry visit (SEPHIA). Referral to primary care.

*Collection of registry data for the SWEDEHEART registry.

As shown in Table 3, there were three time-points for collection of registry data: in-hospital data collected by a coronary care unit nurse and registered in the RIKS-HIA sub-registry, followed by two outpatient registry visits where information was collected by a cardiac rehabilitation nurse and registered in the SEPHIA sub-registry. Apart from the visits shown in Table 3, for both groups, additional visits and telephone contacts were offered to patients according to need.

Paper II

The study was a survey-based study presenting the results of the Perfect-CR questionnaire which reflected everyday operations and work routines at 78 Swedish cardiac rehabilitation centres. The centres were asked to reply as to reflect their work routines during the year 2016 (Figure 7).

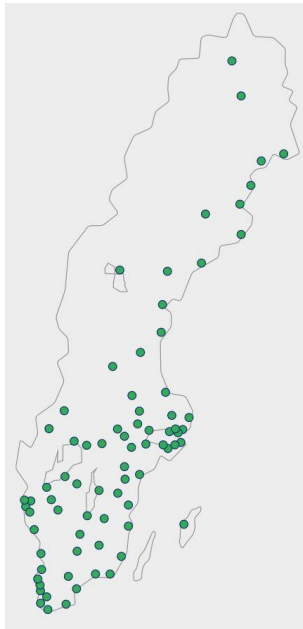

Figure 7. Participating hospitals in the SWEDEHEART registry in 2016.
A map of Sweden with a mark for hospitals that participated in the SWEDEHEART registry during 2016. Reprint permission granted from SWEDEHEART and Uppsala Clinical Research Center.

Paper III

The study was an unblinded parallel multicentre RCT taking place at cardiac rehabilitation centres at the University Hospitals in Malmö, Lund and Umeå, Sweden. A study protocol was published in 2019 (130). The study was reported according to the Consolidated Standards of Reporting Trials (CONSORT) 2010 statement (131).

Patient inclusion started in April 2016 and was finalised in April 2018. The follow-up period was completed in June 2019.

The inclusion criteria were age 18-74 years, having suffered an MI within the last two weeks, owning a smartphone and/or having access to the internet via a computer or tablet, and being able to handle the software. The exclusion criteria were having an expected survival of less than one year, dementia, severe psychiatric illness or drug abuse, severe physical handicap limiting the patients´ ability to take part in a centre-based exCR, inability to speak or understand Swedish, and having a three-vessel or left main CAD requiring CABG.

Eligibility screening and inclusion was performed in-hospital within two weeks of the index MI. Local study coordinators (physicians, nurses, or physiotherapists)

provided patients with information about the study and obtained a written informed consent. Randomization was performed using opaque sealed envelopes. The envelopes were prepared by a member of the research team, and then mixed by another member. Upon recruitment, baseline questionnaires were administered. A total of 150 patients were recruited and randomised either to an intervention group or a control group. During the randomization process 101 patients were randomized to the intervention group and 49 to the control group instead of the planned 100:50, this was because the randomization process was not central but local, meaning that each centre recruited patients until a total of 150 was reached.

Patients in both groups took part in the local cardiac rehabilitation programme. Additionally, the intervention group had access to a web-based application (LifePod ® support software, Cross Technology Solution AB, Lund, Sweden) for the first 25 weeks of the cardiac rehabilitation programme. The first follow-up visit at all centres was approximately 2 weeks post-discharge (initial assessment), followed by pre-specified SEPHIA registry visits at 2-4 weeks, 6-10 weeks, 4-6 months, and 12-14 months post-MI (Figure 8).

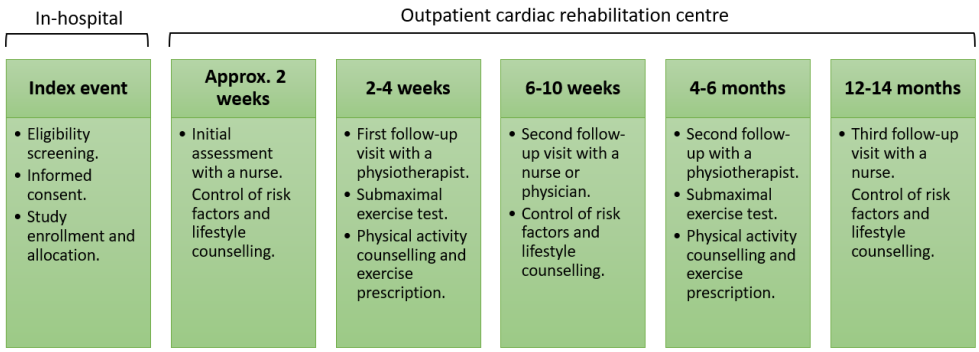

Figure 8. The timeline for the follow-up of post-MI patients in Paper III.
The figure displays the specific timepoint for follow-up of patients in Paper III and the purpose of the follow-up visits.

The LifePod ® support software was a web-based mobile device application specifically designed to support adherence to lifestyle advice and self-control of risk factors. The software contained two separate interfaces: one for the patient and one for the treating healthcare professionals (Figure 9). In the patient interface, the patient could log information about diet, physical activity and exercise, weight, heart rate, BP, and smoking, as well as symptoms related to CAD and intake of medication. The patient could compare his or her own data to guideline-recommended targets and received recommendations and positive feedback on healthy lifestyle choices. In the medical interface assessed by the cardiac rehabilitation staff, the system ranked patients giving high priority to, for example, patients reporting chest pain or out-of-range BP. The medical interface was routinely reviewed by a cardiac rehabilitation nurse twice weekly.

Figure 9. Screen shots of the LifePod ® patient and medical interfaces.
Screen shots of the LifePod ® patient interface above and the medical interface below. The Lifepod ® software could be accessed through a smartphone, tablet, or computer.

Paper IV

The study was an observational registry- and survey-based study with data derived from the Perfect-CR survey, the SWEDEHEART registry and Statistics Sweden.

Organizational predictors were derived from the Perfect-CR survey and reflected cardiac rehabilitation centres´ work routines and organization during the year 2016.

The patient population used in the study was defined by the discharge date after hospital admission due to MI (01.11.2015 to 31.10.2016). The timeframe was chosen to match the time during which the patients attended cardiac rehabilitation (the first months after discharge) to the answers in the Perfect CR survey. Inclusion criteria were surviving a type 1 MI (caused by an acute atherothrombotic coronary event), and age <74 years (the SWEDEHEART registry´s cut-off age at the time).

Patient-level data was derived from the SWEDEHEART registry and Statistics Sweden. The SWEDEHEART registry provided baseline characteristics including

age, gender, and comorbidities, as well as one-year outcome data. Statistics Sweden provided data on country of birth, employment status, marital status, education attainment, and household disposable income (132). A full list of variables and their definitions can be seen in Supplementary material 2.

Geographical distance (kilometres) to the cardiac rehabilitation centre was estimated using longitude and latitude coordinates for the centre of each patient's postal code area (derived from the SWEDEHEART registry) as a proxy for their address, from which the driving route to the follow-up centre was calculated by a commercially available algorithm using Google Maps (133).

Statistics and endpoints

Statistical programmes

For analyses of data in **Paper I-IV** SPSS statistical software (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) was used.

For **Paper IV**, SPSS was used for calculations of baseline characteristics and the statistical software SIMCA P+ (version 15.0.2.0, Sartorius Stedim Data Analytics AB, MKS, Umeå, Sweden) was used for calculation of outcomes.

Endpoints and their calculations

Paper I

Primary endpoints were delta values (δ) between first and second follow-up for BP (mmHg), BMI (kg/m^2), LDL-, HDL- and total cholesterol, and triglycerides (mmol/L). Delta values (δ) were the differences in patient outcomes between registry visits. Smoking and self-reported physical activity were compared by direct measurements at the second follow-up visit (Figure 10).

Blood-lipids samples were analysed with accredited methods at the Clinical Biochemistry department of Skåne University Hospital Malmö. BP was measured with a manual sphygmomanometer after a 5-min rest with patient in sitting position. Weight was measured in light indoor clothing and BMI calculated. Smoking cessation was self-reported and defined as being smoke-free for ≥1 month. For physical activity patients were asked how many days during the last week they had performed any physical activity at least 30 min per day corresponding to a brisk walk.

Secondary endpoints reflected 1) workload and organisation (number of follow-up visits and telephone contacts to the centre) and 2) number of hospital readmissions.

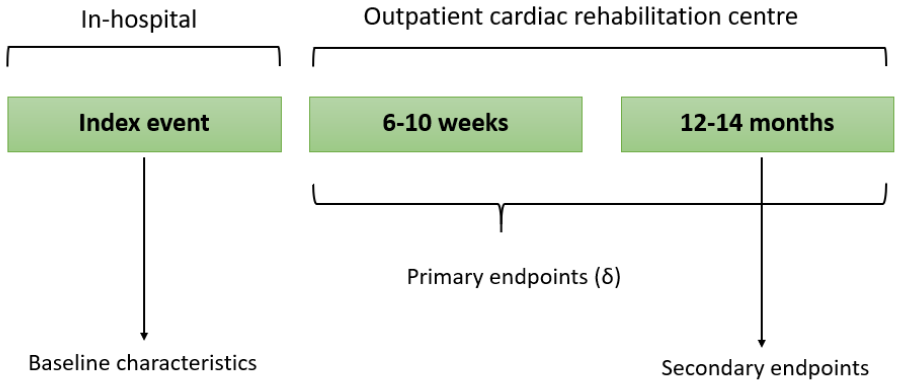

Figure 10. Diagram of endpoint measurements in Paper I.
Diagram showing the time points for measurement of primary and secondary outcomes in Paper I. Delta values were calculated between indicated time intervals for the primary endpoints, and secondary endpoints were measured at the end of the study period.

Baseline characteristics were described with means ± standard deviation (SD), or total numbers and percentages. Differences between group means were assessed using independent samples-t-test for continuous variables and chi-square test for categorical variables.

Regression analysis was used to compare outcomes between the two groups. For continuous variables, a multivariable linear regression analysis was used adjusting for age, gender, BMI, participation in exCR, comorbidities including prior CAD and DM, and cardioprotective medication at discharge. For categorical variables, logistic regression was used, adjusting for the same variables.

Paper II

The paper was descriptive, and no endpoints were defined.

Descriptive statistics were applied: means (±SD) for normally distributed continuous variables, medians (q1, q3) for non-normally distributed continuous variables, and as total numbers and percentages for categorical variables.

Paper III

The primary outcome was change in submaximal exercise capacity (Watts, W) measured at the two consecutive submaximal exercise tests at 2-4 weeks and 4-6 months (Figure 11). Exercise capacity was chosen as the primary outcome since it was the only objectively measured lifestyle-related outcome.

Secondary outcomes were changes in total-, LDL- and, HDL-cholesterol, triglycerides (mmol/L), fasting plasma-glucose (mmol/L) and haemoglobin A1c (HbA1c) (mmol/mol), SBP and diastolic BP (DBP) (mmHg), and BMI (kg/m^2), as well as dietary habits and physical activity. Smoking status was obtained by direct measurements during follow-up visits.

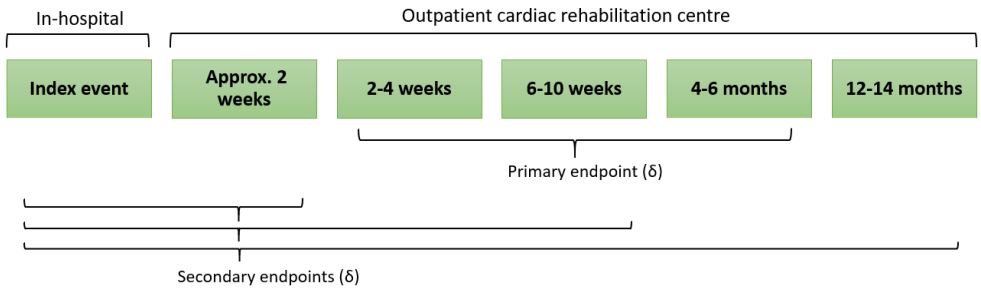

Figure 11. Diagram of endpoint measurements in Paper III.

Diagram showing the time points for measurement of primary and secondary outcomes in Paper III. Delta values were calculated between indicated time intervals, except for smoking status which was obatined by direct measurements. The diagram does not include uptake and adherance which was measured at 25 weeks.

Blood-lipids, fasting plasma-glucose, and HbA1c were analysed with accredited methods at each hospital. BP was measured with a manual sphygmomanometer after a 5-min rest with patient in sitting position. Weight was measured in light indoor clothing and BMI calculated. Smoking cessation was self-reported, at the first follow-up visit at approximately 2 weeks it was defined as being smoke-free until the time of the visit, after which it was defined as being smoke-free for ≥1 month. Diet was evaluated using a four-item questionnaire, adapted from national guidelines for management of unhealthy lifestyle in the general population (134). The questions aimed to quantify the amount of vegetables, fruit, fish, and sweets consumed. Each question had four possible answers giving zero to three points. A high number of points indicated frequent consumption of vegetables, fruits and fish and infrequent consumption of sweets. The scores for each question were subsequently added, forming a healthy diet index (0-12 points). Self-reported physical activity was evaluated using two sets of questionnaires: “Haskell’s questions on physical activity and exercise ”, that evaluates number of days performing at least 30 minute of physical activity and at least 20 minute of exercise training during the latest week (135); and “Frändin/Grimby physical activity questionnaire” aimed to evaluate the level of physical activity a person achieved in the last week on a grading scale of one to six (136).

Secondary outcomes also included uptake and adherence to the web-based application. Uptake was defined as the proportion of patients who logged in at least once and adherence was defined as the proportion of patients registering data at least twice per week on a weekly basis throughout the intervention period.

Baseline characteristics were presented as means (±SD) for normally distributed continuous variables, medians (q1, q3) for non-normally distributed continuous variables, and as total numbers and percentages for categorical variables.

To compare outcome measures between the groups for continuous variables, independent samples-t test and Mann-Whitney test (unadjusted) and univariate ANOVA (ANalysis Of VAriance) were used, adjusting for age, gender, weight, prior CAD, prior DM, and smoking status at the time of index MI. For categorical variables, chi-square test (unadjusted) and a logistic regression analysis adjusting for the same variables, were used. For within-group comparisons, paired-t-test was used for normally distributed variables and Wilcoxon-rank test for skewed data.

Paper IV

Outcomes for **Paper IV** were secondary preventive risk factor targets for LDL-cholesterol (<1.8 mmol/L), BP (<140/90 mmHg), and self-reported smoking abstinence (yes/no) one-year after suffering an MI for patients attending cardiac rehabilitation in Sweden. LDL-cholesterol and BP goal attainment were dichotomized and defined according to the 2016 European guidelines for therapeutic targets used at the time of the study (5). Smoking was self-reported and defined as being smoke-free for ≥1 month.

Organizational and patient-level data were merged based on the cardiac rehabilitation centre at which each patient was followed.

Baseline characteristics were presented as means (±SD) for normally distributed continuous variables, medians (q1, q3) for non-normally distributed continuous variables, and as total numbers and percentages for categorical variables. Differences between groups at baseline were assessed using independent samples-t-test for continuous variables and chi-square test for categorical variables.

A multivariable discriminant analysis was performed by Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA). OPLS is a is a variant of partial least squares (PLS) analysis which in turn is an extension of principal components analysis. PLS regression is originally a type of regression analysis with continuous dependent variables. A discriminant analysis, as was used in our study, uses dichotomised variables (two groups). OPLS-DA is a supervised data projection method used to relate a set of predictor variables (X) to one or more observations (i.e., dependent variables). In our study we analysed one observation at a time. OPLS-DA uses a non-linear iterative partial least squares (NIPALS) algorithm that allows analysis of many variables in comparison to number of observations (137). OPLS-DA separates the systematic variation into two parts, one that is correlated (predictive, X-axis) and another part that is uncorrelated (orthogonal, Y-axis) to the observation. The objective is to improve interpretation of the PLS analysis and reduce its complexity by removing the within group variation that is orthogonal to

X. It results in systematic and correlated components being calculated and extracted (138).

The risk of overfitting (that an analysis corresponds too closely to a dataset, and can fail to fit additional data reliably) is reduced by cross-validation (138). Cross-validation is a resampling technique.

The OPLS-DA computes the influence of every X-variable on separation of the two groups providing Variables of Importance for the Projection (VIPs) of grouping separation as well as the loadings of the variables (138). VIP is a weighted sum of the influence of individual X-variables on the model. If all X-variables had the same contribution to the model, they would have a VIP value equal to 1. VIP values >1 are the most relevant variables, and VIP values <0.5 are considered irrelevant variables. For our analysis, a VIP value with a value >0.8 with a confidence interval (CI) not including zero was considered to have influence in the projection and, thus, meaningful. The VIP values are presented in results together with standard error (SE), as indicators of the CI. To aid in interpretation of the VIP value the loading value was considered. The loading shows what influence an original predictor variable (X) had on the various principal components (how the values were projected onto the principal components). Thus, the loading indicated whether the predictor variables were positive predictors or negative predictors of outcomes.

Ethical considerations

The studies presented in this thesis used registry data. In using registry data, individual integrity of the study population needs ethical consideration. Other ethical considerations include those related to study conduct, study quality, risks and benefits and the need for new evidence.

To aid in planning and conducting medical research ethical, guidelines have been developed to promote high standards of ethical behaviour and care by physicians. Guidelines on research ethics were taken up in 1964 by the World Medical Association in the Declaration of Helsinki. The declaration was developed as a statement of ethical principles for medical research involving human subjects, including research on identifiable human data (139). In addition to the Declaration of Helsinki, the Swedish Research Council has published guidelines on research conduct and ethics (140). National laws are also applicable to the conduct of medical research, for example, the Ethical Review of Research Involving Humans (SFS 2003:460) of Sweden and the General Data Protection Regulation of the European Union (141).

All studies presented in this thesis were reviewed by The Regional Ethical Review board in Lund and approved and received the following registration numbers (Dnr):

- **Paper I**: 2016/494.
- **Paper II** and **IV**: 2336-001.
- **Paper III**: 2016/5.

The studies in **Papers I, III** and **IV** used data retrieved from SWEDHEART (see patients' rights page 48).

The study in **Paper III** was an RCT and all patients provided a written informed consent for participation in the study.

Results

Paper I

Baseline characteristics of all 217 patients are displayed in Table 4. The groups were similar, the only significant difference was the level of total cholesterol, which was lower in the tailored, nurse-led group.

Tabel 4. Baseline characteristics.

	Traditional care	Tailored nurse-led care	P-value
Number of patients:	105	112	
Demographics:			
Males, n (%)	57 (71)	83 (74)	0.67
Age, years	61.7±9.1	61.8±8.0	0.10
Risk factors:			
Diabetes Mellitus, n (%)	33 (31)	21 (19)	0.10
Active smoker, n (%)	43 (41)	40 (36)	0.35
SBP, mmHg	149.9±32.2	153.7±24.2	0.33
DBP, mmHg	87.1±17.3	87.4±15.2	0.90
BMI, kg/m2	27.3±4.5	27.9±4.5	0.37
Total cholesterol, mmol/L	5.0±1.2	4.6±1.0	0.01
LDL, mmol/L	3.0±1.2	2.7±0.9	0.45
HDL, mmol/L	1.2±0.4	1.2±0.4	0.19
TG, mmol/L	1.8±1.3	1.5±0.7	0.07
LVEF at the time of index event			0.09
Normal (≥50%), n (%)	68 (65)	88 (79)	
Mildly decreased (40-49%), n (%)	20 (19)	17 (15)	
Moderately decreased (30-39%), n (%)	8 (8)	4 (4)	
Severely decreased (≤29%), n (%)	3 (3)	0 (0)	
History of CAD:			
MI, PCI or CABG, n (%)	19 (18)	22 (20)	0.83
Type of myocardial infarction			
NSTEMI, n (%)	74 (70)	73 (65)	0.40
STEMI, n (%)	31 (30)	38 (34)	0.49

Number of vessels affected			0.44
No significant stenosis, n (%)	7 (16)	4 (10)	
1-2 affected vessels, n (%)	23 (51)	27 (64)	
3 affected vessels or left main stenosis, n (%)	15 (33)	11 (26)	
In-hospital treatment			
PCI, n (%)	81 (77)	85 (76)	0.62
CABG, n (%)	12 (11)	20 (18)	0.25
Pharmacological treatment at hospital discharge:			
Platelet inhibitors, n (%)	105 (100)	111 (99)	0.33
Statins, n (%)	104 (99)	110 (98)	0.97
Ezetimibe, n (%)	1 (1)	1 (1)	0.62
ACEi or ARB, n (%)	103 (98)	103 (92)	0.06
B-blockers, n (%)	91 (87)	96 (86)	0.62

SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglycerides; LVEF, left ventricular ejection fraction; CAD, coronary artery disease; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; NSTEMI, non-ST elevation myocardial infarct; STEMI, ST elevation myocardial infarct; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker.

Primary endpoints

Of the primary endpoints there was an observed significant reduction in SBP (-2.4±16.0 vs. 4.3±20.3, p=0.01), LDL- (-0.1±0.8 vs. 0.2±0.9, p=0.02) and total cholesterol (-0.1±0.8 vs. 0.4±1.0, p=0.02) in favour of the tailored, nurse-led group between the first (6-10 weeks) and second (12-14 month) follow-up visits (Table 5).

Active smokers at baseline were more often abstinent at the second follow-up visit in the tailored, nurse-led group: n=25 out of 40 (63%) vs. n=18 out of 43 (42%); OR 0.32 (CI 0.1-1.0), p=0.05.

Self-reported physical activity was lower in the tailored, nurse-led group: 1.3 (±2.1) vs. 1.9 (±2.3) days during the last week performing at least 30 minutes of moderate physical activity, p=0.04. However, as was documented at the 12-14-month follow-up visit, the patients in the tailored, nurse-led group more often participated in centre-based exercise training; n=83 (74%) vs. n=64 (61%), p=0.04.

Secondary endpoints

Compared to the traditional group significantly fewer patient in the tailored, nurse-led group had a follow-up visits with a cardiologist (n=67 (60%) vs. n=103 (98%), p<0.001) (Figure 12). The number of nurse visits was the same with 2.4 visits/patient/year in the tailored nurse-led group vs. 2.6 visits/patient/year in the traditional group (p=0.30). The number of telephone contacts was higher in the tailored nurse-led group (5.8 vs. 4.1 contacts/patient/year, p=0.02).

There was a non-significant trend towards more readmissions due to cardiovascular causes (angina, MI, heart failure and stroke) in the traditional group: n = 10 out of 105 (9.5%) vs. n = 4 out of 112 (3.6%) in the tailored nurse-led group, p = 0.10. All four readmissions in the tailored nurse-led group were due to angina and no patients were readmitted due to MI, heart failure or stroke (n = 0 out of 112 (0.0%) vs. n = 8 out of 105 (7.6%) p = 0.003).

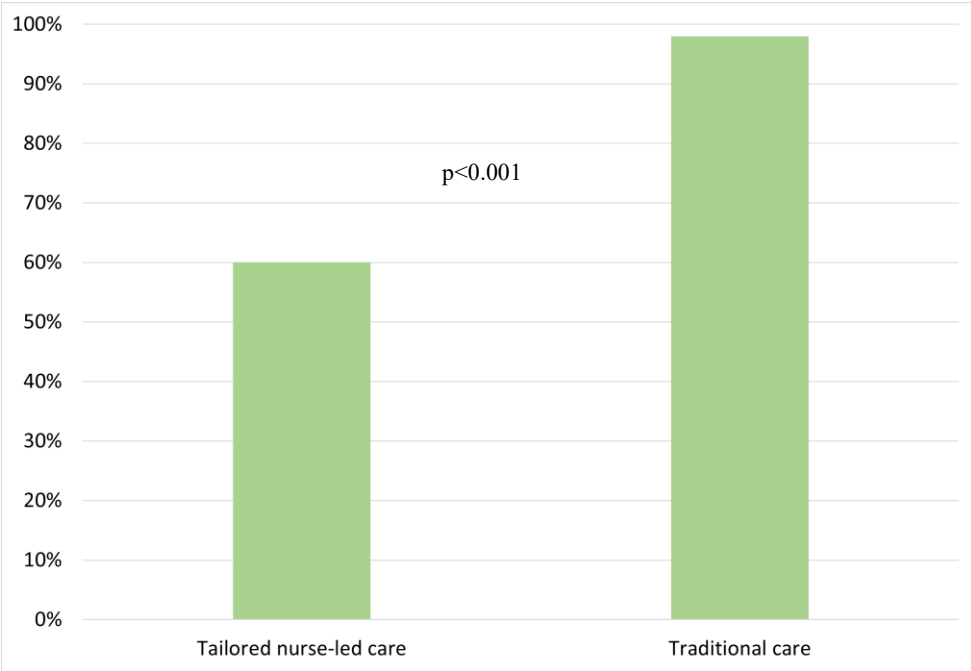

Figure 12. Percentage of follow-up visits with a cardiologist during the follow-up period.
Bar chart of the number of cardiologist visits during the follow-up period showing significantly fewer visits in the group receiving tailored nurse-led care.

Table 5. Outcome measurements at first and second follow-up visits. Differences between the first and second visit values (delta) and comparisons of delta values between the groups were performed using regression analysis.

	Traditional care			Tailored, nurse-led care			
	First visit	**Second visit**	**Difference (delta)**	**First visit**	**Second visit**	**Difference (delta)**	**P for difference**
SBP (mmHg)	129.2±18.5	133.5±21.0	+4.3±20.3	132.8±20.2	130.7±15.1	-2.4±16.0	0.01
DBP (mmHg)	79.8±10.6	79.9±10.3	+0.1±11.6	81.7±10.0	79.1±8.9	-2.6±9.3	0.18
BMI (kg/m^2)	27.8±4.6	26.2±3.8	-0.5±1.5	30.7±2.5	28.3±3.9	-0.1±1.8	0.15
Total cholesterol (mmol/L)	3.5±0.68	3.8±0.98	+0.4±1.0	3.6±0.83	3.6±0.93	-0.1±0.8	0.02
LDL (mmol/L)	1.6±0.59	1.8±0.91	+0.2±0.9	1.8±0.66	1.6±0.70	-0.1±0.7	0.02
HDL (mmol/L)	1.2±0.40	1.4±0.43	+0.1±0.3	1.2±0.41	1.3±0.43	+0.1±0.2	0.06
TG (mmol/L)	1.36±0.82	1.35±0.92	-0.01±0.8	1.35±0.75	1.31±0.79	-0.04±0.7	0.59

Results are presented as numbers (n) and percentages (%) or means (±SD) and p-values for difference.
SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LDL, low density lipoprotein; HDL, high density lipoprotein; TG, triglycerides

Paper II

Response rate

All 79 cardiac rehabilitation centres completed the questionnaire, giving a 100% (n=78) response rate. As previously stated, one centre was excluded from further analysis as it closed its operation only weeks after the questionnaire was sent out. Out of the remaining 78 centres, at 88% (n=69) of centres, two or more professions jointly answered the questionnaire. The most common profession to answer the questionnaire was a nurse (96%, n=75), followed by a physiotherapist (80%, n=62) and, lastly, a cardiologist (47%, n=37).

In-hospital work routines

Most centres (95%, n=74) reported initiating their cardiac rehabilitation programmes while patients were still admitted to hospital. The most common profession to meet with the patients while in-hospital was a physiotherapist (78%, n=61) followed by a nurse (23%, n=18) and at 17% (n=13) of centres patients met with both professions.

Table 6 displays in-hospital work routines, programme intensity and staffing. It shows that most centres reported delivering written information on follow-up structure and content of the cardiac rehabilitation programme, and that the duration and staffing of the programmes varied.

Table 6. Characteristics of cardiac rehabilitation programmes.

Programme characteristics	
In-hospital work routines	**n (%)**
Patients met with a physiotherapist to discuss the physical activity and exercise training components of CR	61 (78)
Patients met with a CR nurse to discuss the CR programme	18 (23)
Information received on CR programme structure at discharge consultation (i.e. time of first assessment, personnel involved in CR and length of follow-up)	
• Written personalised information	64 (82)
• Written general information	58 (74)
• Verbal information	70 (90)
• Referral to website for information	9 (12)
Information received on therapeutic goals on SBP and LDL cholesterol at discharge consultation	
• Written personalised information	7 (9)
• Written general information	34 (44)
• Verbal information	35 (45)
• Referral to website for information	3 (4)
Information received on lifestyle goals (i.e. diet, smoking cessation, physical activity/exercise) at discharge consultation	
• Written personalised information	21 (27)
• Written general information	54 (69)
• Verbal information	63 (81)
• Referral to website for information	6 (8)
Information received on current medical regime at discharge consultation	
• Written personalised information	72 (93)
• Written general information	39 (50)
• Verbal information	64 (82)
• Referral to website for information	5 (6)
Partners/spouses were invited to attend the physician consultation at discharge	12 (15)
Intensity of CR programmes	**Median (q1, q3)**
Number of *hours* with a CR nurse per patient	3 (2, 4)
Number of *hours* with a cardiologist per patient	1 (1, 2)
Number of *hours* patient was offered interactive group education	6 (4, 8)
Number of *sessions* patient was offered centre-based exercise training	24 (24, 32)
Total length of CR programme (*months*)	6.5 (2.5, 12)
Personnel	**n (%)**
Nurses	
• Nurses are a part of the CR team	77 (99)
• Nursing staff has been unchanged during the last two years	49 (63)
• Nurses work only at the CR centre	42 (54)
Physicians	
• A cardiologist is a part of CR team	76 (98)

• Physician staff has been unchanged during the last two years	54 (69)
Physiotherapist	
• Physiotherapists are a part of the CR team	76 (98)
• Physiotherapist staff has been unchanged during the last two years	30 (39)
Other allied healthcare professions included in the CR team	
• A social services expert	69 (89)
• A dietician	66 (85)
• An occupational therapist	30 (38)
• A psychologist	11 (14)
Number of MI patients/year per full-time employed profession	**Median (q1, q3)**
Physiotherapist	99 (63, 150)
Nurse	78 (50, 138)

Results are presented as numbers (n) and percentages (%) or medians (q1, q3).
CR, cardiac rehabilitation; SBP, systolic blood pressure; LDL, low density lipoprotein; MI, myocardial infarction.

Programme structure and staffing

Programme duration varied from 2 to 14 months (Table 6). At 89% (n=69) of centres patients were offered at least one consultation with a physician while the remaining 12% (n=9) provided a consultation with a physician according to patient needs. Home-based cardiac rehabilitation was offered at 10% (n=8) of centres.

A medical director was responsible for the cardiac rehabilitation programme at 76% (n=59) of centres. All but three centres reported having all three core professions (cardiologist, nurse, and physiotherapist) in their cardiac rehabilitation team but the number of centres employing other allied professions varied (Table 6).

Outpatient work routines

Initial outpatient assessment

All centres reported offering patients an individual post-discharge assessment with a nurse and 90% (n=70) of centres reported doing so within the recommended three weeks from discharge. The content of the initial assessment with a cardiac rehabilitation nurse varied and can be seen in Table 7.

Table 7. Content of the initial outpatient assessment by a cardiac rehabilitation nurse.

Topics included	n (%)
Self-reported risk factor evaluation	
Assessment of smoking status	78 (100)
Physical activity counselling	77 (99)
Diet/nutritional counselling	77 (99)
Smoking cessation counselling (if suitable)	77 (99)
Assessment of exercise training and physical activity	76 (97)
Assessment of diet/nutrition	74 (95)
Exercise training counselling	66 (85)
Assessment of alcohol consumption	66 (85)
Counselling on alcohol consumption (if suitable)	65 (83)
Objectively measured risk factor evaluation	
Blood pressure measurement	77 (99)
Adjustment of antihypertensive medication (if suitable)	69 (88)
Counselling on weight loss (if suitable)	62 (80)
Measurement of blood-lipids or assessment of in-hospital values	60 (77)
Measurement of weight	59 (76)
Measurement of fasting plasma-glucose and/or HbA1c or assessment of in-hospital values	48 (62)
Measurement of waist circumference	47 (60)
Adjustment of lipid-lowering medication (if suitable)	29 (38)
Psychosocial evaluation	
Verbal assessment of mental health (anxiety, depression and stress)	76 (97)
Mental health counselling (i.e. referral to primary care, social service expert or psychologist)	76 (97)
Assessment of social situation i.e. family support, employments status, economic issues etc.	65 (83)
Structured assessment of mental health (anxiety, depression and stress) using grading scales	11 (14)
Patient information and education	
Review of current medication	78 (100)
The patient receives a written copy of lab values (blood values, blood pressure, etc.)	44 (56)
The patient receives written information on therapeutic goals with regards to risk factors and lifestyle.	36 (46)

Results are presented as numbers (n) and percentages (%).
HbA1c, Haemoglobin A1c.

Interdisciplinary team meetings

Having interdisciplinary team meetings to discuss patient cases was reported to be done at least once a week at 40% (n=31) of centres whilst 58% (n=45) reported discussing patient cases sporadically i.e., when needed.

Meetings to discuss operational matters were reported to be held at least once per year at 77% (n=60) of centres.

Nurse autonomy

Whether cardiac rehabilitation nurses independently adjusted patient medication varied. At 82% (n = 64) of the centres, nurses were authorized to adjust dosage of

antihypertensive treatment (β-blockers, renin–angiotensin–aldosterone system inhibitors, diuretics, and calcium-channel blockers) and statin dose adjustment was authorized at 56% (n = 44).

Programme content

Smoking cessation

To facilitate smoking cessation centres reported the following:

- Recommending nicotine replacement therapy at 87% (n=68) of centres.
- Prescribing varenicline at 51% (n=40) of centres.
- Formal training in smoking cessation counselling was provided for nurses at 59% (n=46) of centres, for physiotherapists at 5% (n=4) of centres and for physicians at none of the centres.

Stress management

Stress management was provided in groups at 26% (n=20) of centres and individually at 35% (n=27) of centres. At 18% (n=14) of centres patients were referred to primary care for stress management and at 32% (n=25) of centres no stress management was offered.

Screening for diabetes mellitus

At 37% (n=29) of centres an OGTT was performed on all or a selected group of patients. In the case of newly diagnosed or uncontrolled DM, most centres (96%, n=75) reported referring patients to primary care or a diabetes outpatient unit. Only 8% (n=6) reported consulting directly with a diabetologist in these cases and in 17% (n=13) of cases the team's own physician would adjust diabetes medication.

Physiotherapy

Post-discharge 83% (n=65) of centres reported offering patients individual counselling with a physiotherapist, 82% (n=64) offered an initial test of physical fitness and 50% (n=39) offered a follow-up test after completion of the exCR programme. Most centres (97%, n=76) offered some form of centre-based exercise training.

Patient education

Most centres offered one-for-all interactive group-based patient education (78%, n=61) and just two centres offered group education adjusted for individual need based on age, gender, or diagnosis. Some offered digital education; 18% (n=14) did so via webpage and 10% (n=8) via mobile applications.

Quality management and clinical audit

All participating centres reported patient outcome data to the SEPHIA sub-registry. When asked whether they used their own SEPHIA data for quality control aiming to improve programme outcomes, 60% (n=47) reported doing so regularly, 33% (n=26) sometimes and 6% (n=5) never.

Patient groups offered participation in cardiac rehabilitation (not included in published paper II)

The Perfect-CR questionnaire included a question regarding which patient groups were offered participation in cardiac rehabilitation at the responding centre. All centres offered cardiac rehabilitation to post-MI patients, but whether other patient groups were offered participation varied widely (Figure 13).

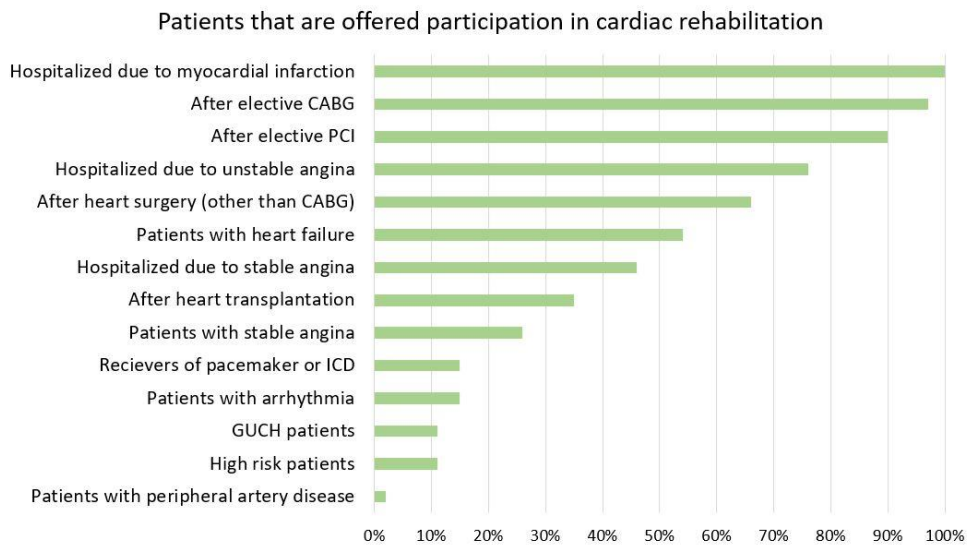

Figure 13. Percentage of centres offering participation in cardiac rehabilitaiton to different patient groups.

A bar chart displaying different groups of patients and the percentage of centres offering participation in cardiac rehabilitation to respective group. CABG; coronary artery bypass grafting, PCI; percutaneous coronary intervention, ICD; implantable cardioverter-defibrillator, GUCH; grown up congential heart disease.

Correlation analysis (not included in published paper II)

An initial correlations analysis was performed in 2017 and presented at the Swedish Heart Association's annual spring meeting and at the ESC annual congress (142). A Perfect CR index was designed, including 37 components (Supplementary material 3) recommended in guidelines as cornerstones of cardiac rehabilitation (18, 74, 143). Centres received 0-30 points based on how many components of the index they fulfilled; their scores are shown in Figure 14. The index gave a general idea of standards of service at Swedish cardiac rehabilitation centres. A limitation of the Perfect-CR index was that for several variables answers of more than one question were combined, that is to receive one index point more than one question needed to provide a specific answer. Also, the index did not include the questionnaire in its entirety.

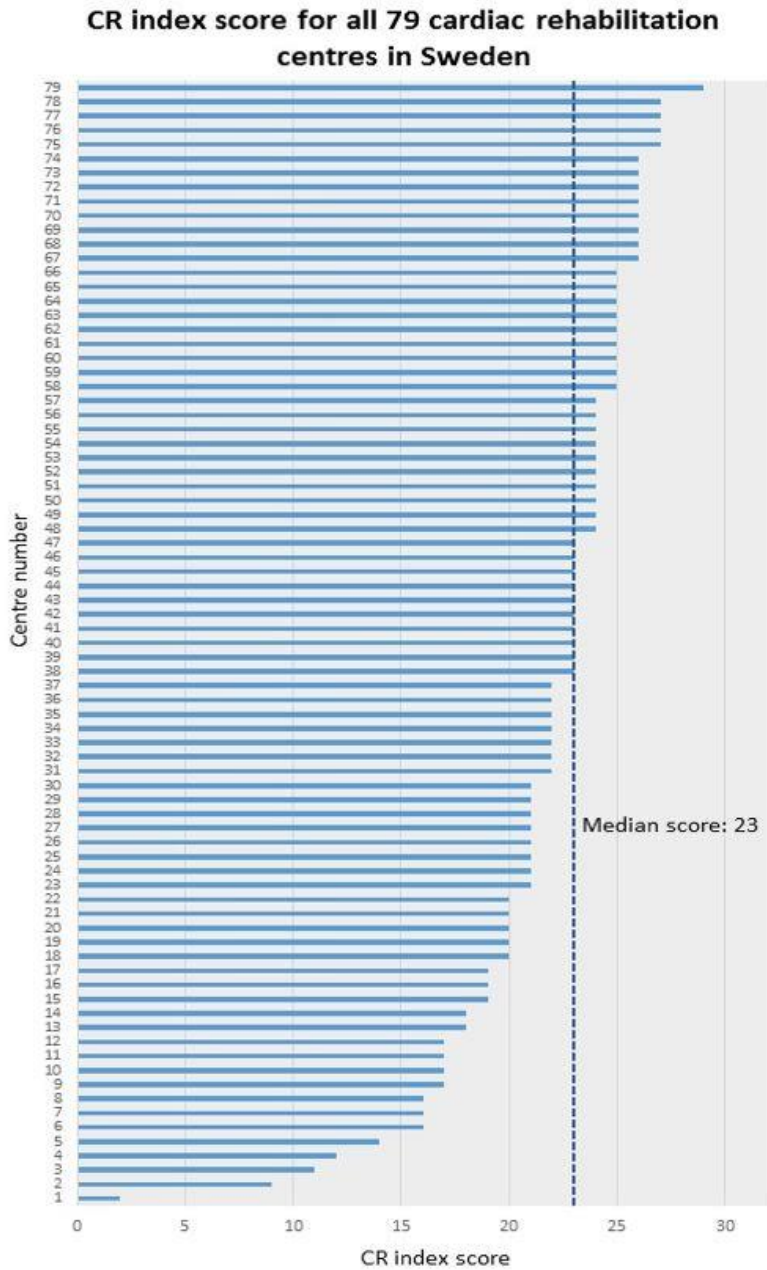

Figure 14. Cardiac rehabilitation index scores.
A bar chart displaying the index scores of the 79 cardiac rehabilitation centres that were included in the Perfect-CR study. Image from a poster presentation from the 2017 Swedish Heart Association's annual spring meeting (142).

The centres median (q1, q3) score was 23 (20, 25) points. A correlation analysis using aggregated data was performed between the index score and SEPHIAs combined outcome measure called Q4. Q4 includes whether therapeutic goals for SBP and LDL-cholesterol were reached, if the patients participated in exCR and if smokers achieved smoking cessation at 12-14 months post-MI. The R-value for the correlation was 0.46 (p=0.0005) and the ten Perfect-CR variables with the strongest correlation, jointly explained 25% of the adjusted variance in Q4 (p=0.01) (Table 8). The limitation of this analysis was its crudeness. By grouping the four Q4 therapeutic goals and compressing the Perfect-CR answers to 30 index points made it impossible to draw a conclusion as to which programme characteristics were related to which therapeutic goal.

Table 8. Components of cardiac rehabilitation programmes that correlate with Q4.

Perfect-CR index item	R	P
The cardiac rehabilitation centre has a medical director (cardiologist)	0.37	0.003
Our nurses independently adjust statins	0.32	0.01
Material on healthy diet is distributed	0.31	0.01
Our nurses have regular rounds with a cardiologist to discuss patient cases	0.27	0.03
Registry data is used on a regular basis to improve quality of care	0.26	0.03
Our patients are provided with written information on risk factor goals prior to hospital discharge	0.25	0.04
Our patients are provided with written information on healthy lifestyle prior to hospital discharge	0.24	0.04
Our patients meet with a physiotherapist prior to hospital discharge	0.22	0.05
We have had low employee turnover in the cardiac rehabilitation team for the last two years (all or most of the staff are the same)	0.22	0.06
Our nurses independently adjust blood pressure medication	0.20	0.08

Paper III

The group size (n) was based on a sample size calculation (116). With a power of 90%, a two-sided significance level of 0.05, and mean difference between the groups of ≥10 W (± 20 W) the estimated sample size was 150 patients. Because of expected loss of adherence to the web-based application an allocation ratio of 1:2 was chosen in the usual care vs. the intervention groups.

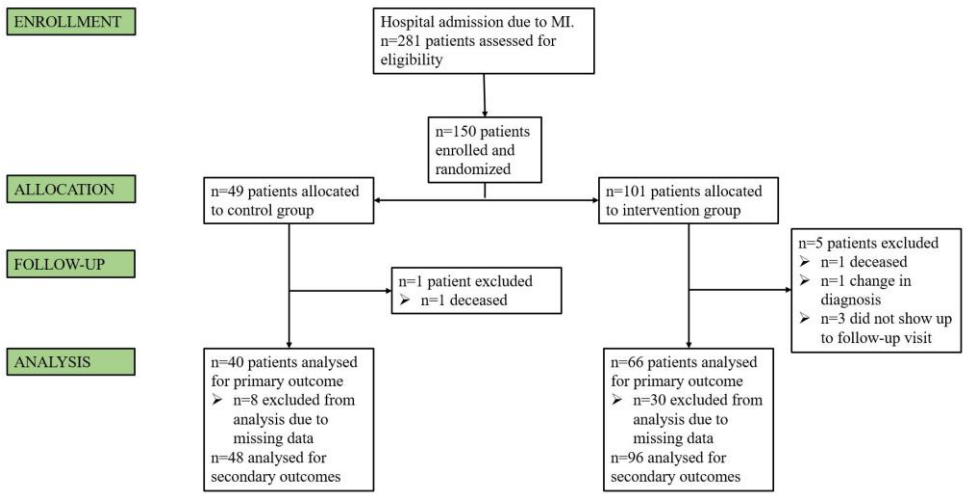

Figure 15. Patient recruitment flow-chart.

Flow chart displaying the recruitment process and flow of participants in the usual care (control) and intervention groups.

As seen in Table 9 the intervention group had a somewhat higher prevalence of comorbidities, a higher SBP and were more often already taking cardioprotective medication in comparison to the usual care group.

Table 9. Baseline characteristics

	Intervention n=101	Usual care n=49
Age, years, mean±SD	60.0±8.9	61.1±8.6
Male gender, n (%)	84 (83.2)	36 (73.5)
Active smoker, n (%)	22 (22.0)	11 (22.4)
Physiological and laboratory measures	**(mean±SD or median (q1, q3)**	
SBP (mmHg)	150.0±27.6	142.9±25.5
DBP (mmHg)	88.5±14.6	86.8±14.8
Waist circumference (cm)	104.9±12.9	104.5±13.9
Weight (kg)	86.3±15.1	85.3±16.2
BMI (kg(m^2)	27 (25, 30)	27 (25, 29)
Total cholesterol (mmol/L)	4.7±1.1	4.9±1.1
LDL (mmol/L)	2.8±0.9	3.0±1.0
TG (mmol/L)	1.4 (0.9, 2.1)	1.4 (1.0, 1.9)
HDL (mmol/L)	1.2 (0.9, 1.4)	1.2 (0.9, 1.4)
Fasting plasma glucose (mmol/L)	7.5 (6.4, 9.2)	7.1 (6.2, 8.9)
HbA1c (mmol/mol)	38 (35, 41)	39 (36, 42)
Previous disease, n (%)		
CAD (previous MI, PCI, or CABG)	18 (17.8)	6 (12.2)
Chronic heart failure	5 (4.9)	0 (0.0)
Diabetes mellitus	9 (8.9)	6 (12.2)
Hypertension	42 (41.6)	17 (34.7)
Medication on hospital admission, n (%)		
ACEi and/or ARB	36 (35.6)	12 (24.5)
Statins	24 (23.7)	5 (10.2)
Acetylsalicylic acid	18 (17.8)	5 (10.2)
Betablockers	19 (18.8)	7 (14.3)
Medication at hospital discharge, n (%)		
ACEi and/or ARB	95 (94.5)	46 (93.9)
Statin	100 (99.0)	47 (95.9)
DAPT	100 (99.0)	49 (100)
Betablockers	89 (88.1)	43 (87.8)
Type of myocardial infarction, n (%)		
STEMI	59 (58.4)	24 (48.9)
NSTEMI	41 (40.5)	24 (48.9)

Results are presented as numbers (n) and percentages (%), mean±SD or medians (q1,q3).
SD, standard deviation; SBP systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LDL, low density lipoprotein; TG, triglycerides; HDL, high density lipoprotein; HbA1c, haemoglobin A1c; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention, CABG, coronary artery bypass grafting; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blocker; DAPT, dual antiplatelet therapy; STEMI, ST elevation myocardial infarct; NSTEMI, non-ST elevation myocardial infarction.

Primary endpoint

Because of missing data at the first or second physiotherapy follow-up, only 66 participants in the intervention group and 40 participants in the usual care group qualified for analysis of the primary outcome (Figure 15).

Both groups increased their submaximal exercise capacity significantly between the first and second follow-up measurements. The intervention group increased their exercise capacity from 96.3±29.4 to 110.8±33.7 W ($p<0.001$), and the corresponding values for the usual care group were 96.1±33.7 and 106.5±37.3 W ($p<0.001$). No significant difference was seen between the delta values of the groups (+14.4±19.0 W vs. +10.3±16.1 W, unadjusted CI -11.2-3.0, $p=0.26$, adjusted CI -12.0-2.8, $p=0.22$) (Figure 16).

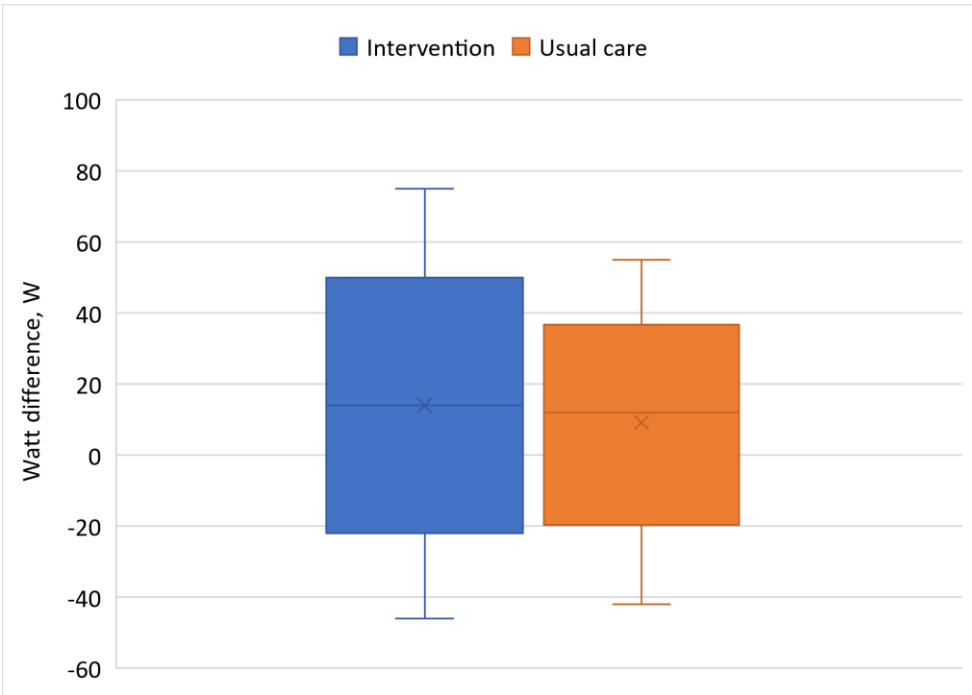

Figure 16. The difference in change of submaximal exercise capacity between the intervention group and the usual care group.

A boxplot of the difference in change of submaximal exercise capacity (in watts, W) between the intervention group and the usual care group. The difference in change in exercise capacity between the groups at follow-up was non-significant.

Secondary endpoints

Results of secondary endpoints are displayed in Tables 10, 11 and 12. In the unadjusted analysis the decrease in SBP between baseline and the 2-week follow-up visit was significantly larger in the intervention group compared to the usual care group. In the adjusted analysis this difference remained significant and was significant for the delta values for both SBP and DBP between baseline and 6-10 weeks follow-up (Tables 10 and 11). The improvement in the healthy diet index score was significantly larger in the intervention group at the 2-week follow-up, largely due to an increased consumption of fish and fruit (Table 10). For other secondary outcomes, no significant differences were seen.

There was an observed numerical difference in the number of active smokers who achieved abstinence. At the 2-week follow-up 73% (n=16 out of 22) of smokers in the intervention group and 54% (n=6 out of 11) of smokers in the usual care group reported to be abstinent from smoking (p adjusted=0.69). At 6-10-weeks the numbers were 73% (n=16 out of 22) vs. 46% (n=5 out of 11) (p adjusted=0.20) and at 12-14 months 58% (n=14 out of 22) vs. 36% (n=4 out of 11) (p adjusted=0.64), respectively. Due to a small sample size (n=33), however, it was not surprising that the difference fell short of statistical significance.

Table 10. Secondary outcome measures (delta values) at the 2-week follow-up.

	Intervention Mean/median difference	Usual care Mean/median difference	P value Unadjusted	P value Adjusted*
Risk factors				
SBP (mmHg)	-27.7±27.6	-16.4±24.1	0.02	0.006
DBP (mmHg)	-13.1±13.0	-11.1±15.1	0.43	0.40
BMI (kg/m^2)	-0.3 (-0.9, 0.5)	-0.1 (-0.7, 0.6)	0.34	0.77**
Self-reported parameters				
Vegetable comsumption	0.4±1.0	0.4±0.8	0.81	0.94
Fruit consumption	0.7±1.0	0.2±1.0	0.03	0.03
Fish consumption	0.8±1.0	0.4±0.8	0.03	0.02
Consumption of sweets	0.5±0.9	0.5±0.9	>0.99	>0.99
Healthy diet index	2.3±2.1	1.4±2.3	0.05	0.03

*adjusted for gender, age, weight, previous coronary artery disease and smoking status at the time of index event.
**not adjusted for weight.
Numbers are presented as mean differences±SD, median differences (q1, q3) and P values for differences.
SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index.

Table 11. Secondary outcome measures (delta values) at the 6-10-week follow-up.

	Intervention Mean/meadian difference	Usual care Mean/meadian difference	P-value Unadjusted	P-value Adjusted*
Risk factors				
SBP (mmHg)	-25.3±27.4	-16.5±27.4	0.08	0.02
DBP (mmHg)	13.4±15.6	-9.1±13.4	0.11	0.05
BMI (kg/m^2)	-0.3 (-1.1, 0.3)	-0.2 (-1,3, 0.3)	0.77	0.39**
Total cholesterol (mmol/L)	-1.5±1.1	-1.6±0.9	0.48	0.37
LDL-cholesterol (mmol/L)	-1.4±0.9	-1.5±0.8	0.28	0.24
HDL-cholesterol (mmol/L)	0.1 (-0.1, 0.2)	0.1 (-0.1, 0.3)	0.80	0.93
Triglycerides (mmol/L)	-0.3 (-0.8, 00)	-0.3 (-0.7, 0.0)	0.93	0.99
Fasting plasma glucose (mmol/L)	-1.4 (-3.3, -0.3)	-0.9 (-2.8, -0.2)	0.81	0.47
Self-reported parameters				
Vegetable consumption	0.3±0.8	0.4 ±1.1	0.74	0.65
Fruit consumption	0.6±1.0	0.5 ±1.1	0.29	0.36
Fish consumption	0.9±1.1	0.8 ±1.1	0.27	0.22
Consumption of sweets	0.3±0.9	0.5 ±1.1	0.27	0.22
Healthy diet index	2.2±2.3	2.1 ±2.6	0.82	0.77

*adjusted for gender, age, weight, previous coronary artery disease and smoking status at the time of index event.
**not adjusted for weight.
Numbers are presented as mean differences ±SD, median differences (q1, q3), P-values for differences.
SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LDL, low-denisty lipoprotein, HDL, high density lipoprotein.

Table 12. Secondary outcome measures (delta values) at the 12-14-month follow-up.

	Intervention Mean/meadian difference	Usual care Mean/median difference	P-value Unadjusted	P-value Adjusted*
Risk factors				
SBP (mmHg)	-24.0±31.1	-17.0±28.3	0.22	0.09
DBP (mmHg)	-12.6±17.6	-11.3±17.1	0.69	0.49
BMI (kg/m^2)	-0.3 (-1.3, 1.0)	-0.5 (-1.2, 0.8)	0.57	0.35**
Total cholesterol (mmol/L)	-1.3±1.2	-1.5±1.1	0.41	0.30
LDL-cholesterol (mmol/L)	-1.2±1.1	-1.4±1.0	0.20	0.21
HDL-cholesterol (mmol/L)	0.1 (0.0, 0.3)	0.1 (0.0, 0.3)	0.89	0.77
Triglycerider (mmol/L)	-0.3 (-0.9, 0.0)	-0.3 (-0.8, 0.8)	0.48	0.98
Fasting plasma glucose (mmol/L)	-1.5 (-3.3, -0.2)	-1.4 (-2.7, 2.0)	0.68	0.40
HbA1c (% per unit)	1.0 (-0.2, 3.0)	2.0 (-0,2, 3.8)	0.68	0.40
Self reported parameters				
Vegetable comsumption	0.3±1.0	0.2±0.7	0.67	0.77
Fruit consumption	0.3±0.8	0.3±0.9	0.92	0.99
Fish consumption	0.6±1.0	0.7±1.0	0.70	0.66
Consumption of sweets	0.4±1.0	0.3±1.1	0.45	0.37
Healthy diet index	1.6±2.2	1.4±2.2	0.69	0.45

*adjusted for gender, age, weight, previous coronary artery disease and smoking status at the time of index event.
**not adjusted for weight.
Numbers are presented as mean differences±SD, median differences (q1, q3) and P-values for differences.
SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LDL, low-denisty lipoprotein, HDL, high density lipoprotein; HbA1c, haemoglobin A1c.

Adherence and uptake

Attendance to cardiac rehabilitation was generally high. Ninety-three percent (n=92) of patients in the intervention group attended the first physiotherapist follow-up visit and 72% (n=71) attended the second. The corresponding percentages for the usual care group were 100% (n=48) and 88% (n=42). During these visits, 69% (n=66) of the intervention group and 83% (n=40) of the usual care group performed submaximal exercise tests at both visits.

Ninety two percent (n=91) of patients in the intervention group attended the 6-10-week follow-up and 97% (n=96) attended the 12–14-month follow-up. The corresponding numbers for the usual care group were 100% (n=48) for both follow-ups.

For the web-application uptake was 86% (n=87 out of 101). Adherence was measured for the 87 patients who continued to log data at least twice per week throughout the study period. As seen in Figure 17 adherence dropped during the trial period. Adherence was highest (92%) at week 1 and it continuously declined to 57% at the end of the trial period (week 25). According to the cardiac rehabilitation nurses at the study centres, reported reasons for stopping use of the web-based

application were mostly related to stress, some experienced a lack of feedback and some experienced too much feedback. However, this was not formally documented.

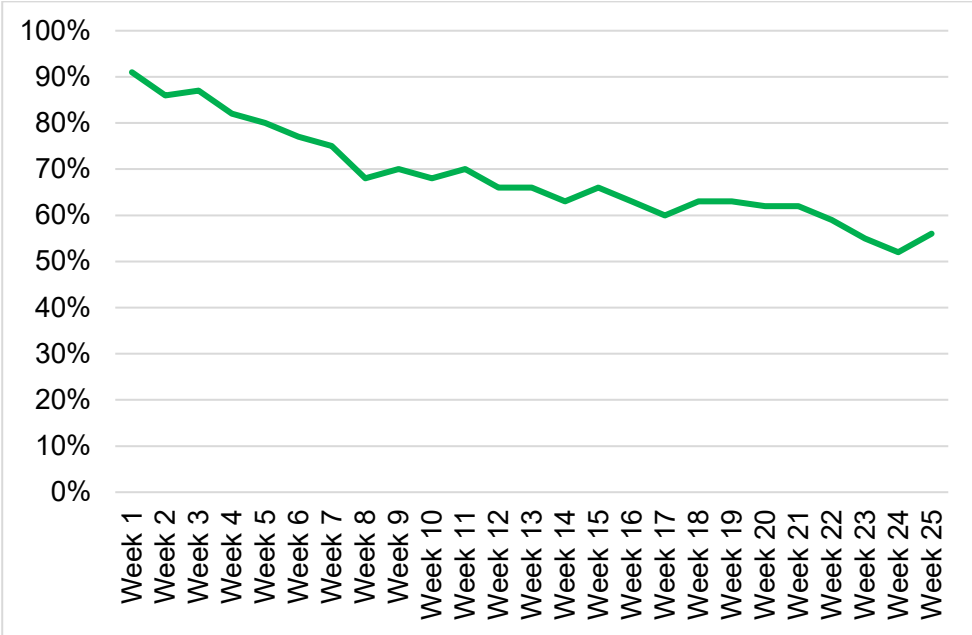

Figure 17. Adherence to the web-application during the trial period.

Percentage of participant logging data to the web-based application at least twice weekly during the 25 week trial period.

The most reported parameter was intake of medication and consumption of vegetables, followed by physical activity (Figure 18).

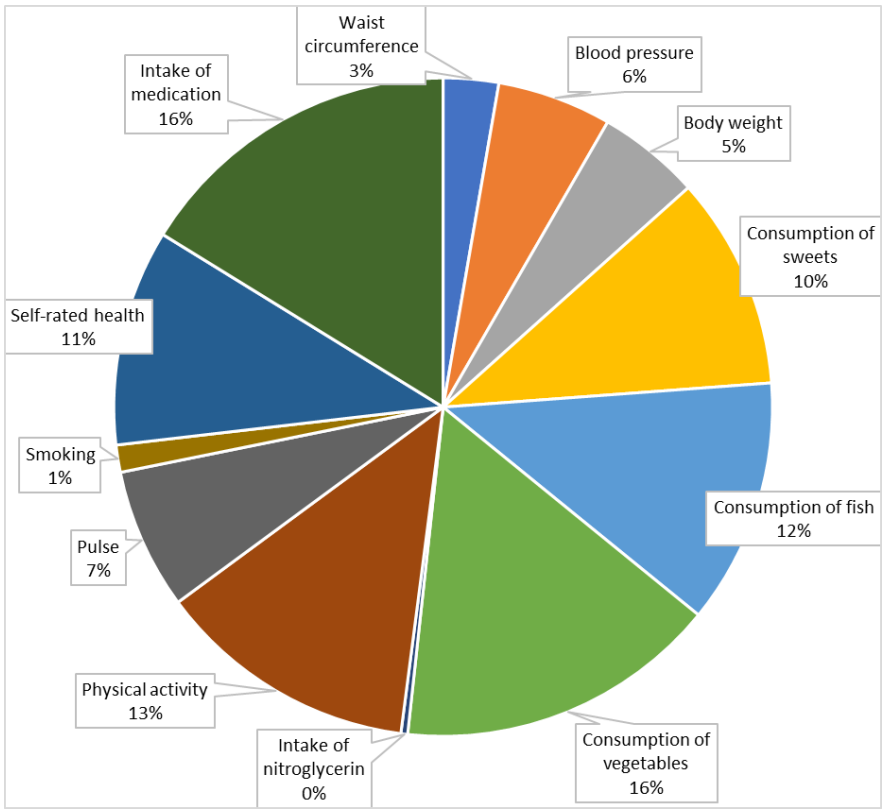

Figure 18. Registered parameters in the web-application.

Percentage of reports per parameter in the web-based application.

Additional analysis

There was no difference in the frequency of deaths due to any cause (n=1 in each group, p=0.62). Rates of rehospitalizations during the 12-14-month follow-up period were also comparable between the groups. Twenty-two (22%) patients in the intervention group and 13 (23%) patients in the usual care group were re-hospitalized due to any cause (p=0.58), and 2 (4%) and 8 (8%) patients were re-hospitalised due to ischemic heart disease, respectively (p=0.35).

Paper IV

Cardiac rehabilitation centre-level data

As in **Paper II** one centre was excluded from the analysis since their operation was shut down only weeks after the Perfect-CR survey was sent out. The decision to exclude the centre was strengthened further when doing the initial principal components analysis as a preparation for the OPLS-DA. The principal components analysis score plot showed that the centre was clearly identified as an outlier (Figure 19).

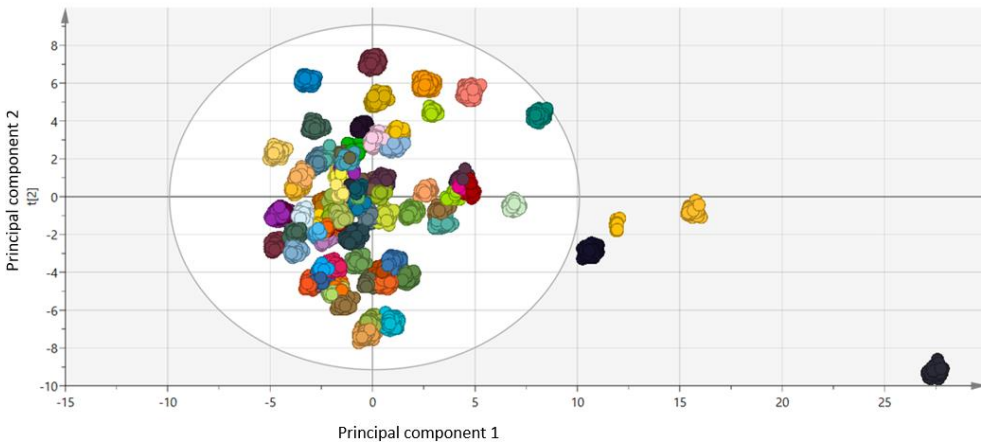

Figure 19. Principal components analysis score plot.

The horizontal component of the score plot contains the data used in Paper IV in its entirety. As the plot showns clear clusters formed. The different color clusters represent the 79 cardiac rehabilitation centres that took part in the Perfect-CR study. The circle presents the Hotelling's t-squared statistic (t2) which is a generalization of Student's t-statistic that is used in multivariate hypothesis.The plot demonstrates one outlier (color black, furtherst to the bottom right) which is the centre which was excluded from further analysis.

The median (q1, q3) percentage of patients per cardiac rehabilitation centre achieving the primary outcome targets were 58.9% (46.7, 65.7) for LDL-cholesterol, 75.4% (69.3, 81.5) for BP and 56.3% (48.5, 63.3) for smoking abstinence.

Detailed descriptive data on organizational variables was presented in **Paper II**. However, for the purpose of synchronizing terminology with the recent position paper from the European Association of Preventive Cardiology (EAPC) some of the variable names have changed slightly in **Paper IV** (75). Organizational variables used in **Paper IV** are displayed in Table 13.

Table 13. Cardiac rehabilitation centre-level data – Organizational variables

Cardiac rehabilitation centre coverage and characteristics		Number of missing/unknown values, n (%)
Centre coverage[a], median % (q1, q3)	81.4 (70.3, 88.0)	7 (9.0)
Hospital-size (size of patient target group), n (%)		0 (0)
<50	4 (5.1)	
51-100	31 (39.7)	
101-150	17 (21.8)	
151-200	10 (12.8)	
>200	16 (20.5)	
University-hospital, n (%)	9 (11.5)	0 (0)
Cardiac rehabilitation centre work routines, n (%)		
In-hospital work routines		
Discharge letter includes lifestyle info	58 (74.4)	0 (0)
Discharge consult protocols available	46 (59.0)	11 (14.1)
Discharge letter includes risk factor info	35 (44.9)	0 (0)
IA scheduled prior to discharge	23 (29.5)	0 (0)
Liaison with CR nurse pre-discharge[b]	18 (23.1)	0 (0)
The CR team and facilities		
Multidisciplinary CR team	75 (96.2)	0 (0)
Psychologist part of team	71 (91.0)	0 (0)
Dietician part of team	66 (84.6)	0 (0)
CR nurses adjust antihypertensive medication	64 (82.1)	0 (0)
Operational CR team meetings	60 (76.9)	0 (0)
Medical director	59 (75.6)	1 (1.2)
Self-reported team spirit[b]	57 (73.1)	1 (1.2)
Protocols for medication adjustment	51 (65.4)	0 (0)
Audit data used for quality control	47 (60.3)	0 (0)
Adequate facilities[b]	55 (70.5)	0 (0)
CR nurses adjust lipid-lowering medication	44 (56.4)	0 (0)
CR nurses – CBT/MI training[b]	35 (44.9)	15 (19.2)
Patient case meetings	31 (39.7)	1 (1.2)
Change in work routines during last year[b]	22 (28.2)	0 (0)
Structure of the CR programme		
IA: Physical activity counselling	75 (96.2)	0 (0)
IA: Psychosocial management	75 (96.2)	0 (0)
IA: Diet/nutritional counselling	73 (93.6)	1 (1.2)
IA: Alcohol counselling	65 (83.3)	2 (2.6)
IA: Vocational support	65 (83.3)	1 (1.2)
Continuity in nurse-patient contact[b]	63 (80.8)	0 (0)
Interactive patient education offered	62 (79.5)	0 (0)
Long-term follow-up of goals[b]	51 (65.4)	0 (0)
Varenicline prescribed	40 (51.3)	0 (0)
Extended opening hours at CR centre	13 (16.7)	0 (0)
IA: Psychosocial screening instruments	11 (14.1)	3 (3.8)

Need for physician consultation adapted	9 (11.5)	0 (0)
Duration of CR programme (months)	6.5 (2.5, 12.0)	12 (15.4)
Exercise-based CR		
1st physio visit (pre exCR assessment)[b]	64 (82.1)	0 (0)
1st physio visit: ex test performed	59 (75.6)	0 (0)
1st physio visit: muscle function test	52 (66.7)	0 (0)
1st physio visit: ex log provided	46 (59.0)	0 (0)
2nd physio visit (close-out post exCR)[b]	44 (56.4)	0 (0)
Home-based exCR is available	44 (56.4)	0 (0)
Physios – CTB/MI training[b]	35 (44.9)	15 (19.2)
2nd physio visit: ex test performed	36 (46.2)	0 (0)
2nd physio visit: muscle function test	31 (39.7)	0 (0)
No of physios/100 patients/year	0.9 (0.6, 1.3)	7 (9.0)
Duration of exercise training programme (hours)	72 (54, 107)	3 (3.8)
Number of different exercise training programme modalities offered	3.2 (±1.4)	0 (0)

Numbers are presented as numbers and percentages (%), means ±SD or medians (q1, q3).
CR, cardiac rehabilitation; LDL-C, low-density lipoprotein cholesterol; BP, blood pressure; CBT, cognitive behavioural therapy; MI, motivational interviewing; IA, initial assessment; exCR, exercise-based cardiac rehabilitation; ex, exercise; physio, physiotherapist.
[a]Number of patients attending one-year follow-up/number of patients eligible for follow-up. [b]Assessed with grading scales ranging from 1 (completely disagree) to 6 (completely agree) responses from 1 to 2 were classified as 'disagree' and responses ranging from 5 to 6 were classified as 'agree'.

Patient inclusion and baseline characteristics

Patient inclusion and flow are displayed in Figure 20. Out of 9165 patients who had suffered an MI during the study period, a total of 7549 (82.3%) patients attended a one-year follow-up at a cardiac rehabilitation centre and were included in the LDL-cholesterol and BP outcome analysis. Attendance was defined as having answered at least two of the following questions at the one-year follow-up visit: having had chest pain, having had shortness of breath, smoking status, snuffing status, physical activity level, presence of DM, current body weight, current waist circumference, diet, current medical regime, quality of life (via EuroQol- 5 Dimension (EQ5D) questionnaire) (144) and/or BP.

Of the 7549 one-year attendees 7250, (96.0%) had registered outcome data for LDL-cholesterol and 7368 had registered outcome data for BP (97,6%). Of the one-year attendees 1810 (24.0%) were females, median age was 64 (57, 70) years, baseline LDL-cholesterol was 3.0±1.1 mmol/L and BP was 150.9±27.5/88.3±16.3 mmHg.

Only active smokers at baseline (n=2169) were included in the analysis of smoking cessation. Data on smoking status at one-year was available for 2167 (99.9%) patients. Of active smokers at baseline with one-year follow-up 635 (29.3%) were female and median age was 61 (54, 67) years. Patient baseline characteristics are displayed in Table 14.

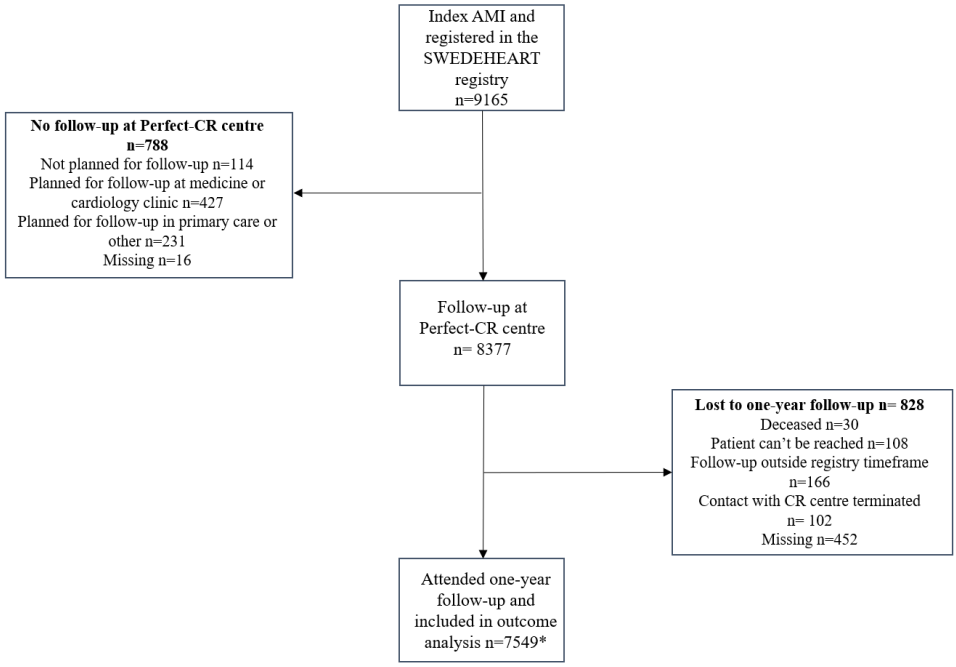

Figure 20. Flow diagram of the patient population.

*Out of the n=7549 that were included in the outcome analysis for LDL-cholesterol and BP, n=2169 were active smokers at baseline that had a one-year follow-up, and were included in the outcome analysis for smoking abstinence.

Table 14. Baseline characteristics

	Patients with index MI	Patients with a one-year follow-up	P-value*	Active smokers with index MI	Active smokers at baseline with one-year follow-up	P-value**
Number of patients (n)	9165	7549		2653	2169	
Demographics						
Age, years	65 (57,70)	64 (57,70)	0.05	61 (54, 68)	61 (54, 67)	0.52
Gender, female, n (%)	2291 (25.0)	1810 (24.0)	0.13	783 (29.5)	635 (29.3)	0.86
Distance between home and CR centre (kilometres)	N/A	13.7 (4.6, 28.8)	N/A	N/A	13.0 (4.6, 27.8)	N/A
Country of birth, n (%)			0.33			0.80
Born in Sweden	7340 (80.1)	6126 (81.1)		1884 (71.0)	1564 (72.1)	
Born in Nordic countries (not Sweden)	458 (5.0)	347 (4.6)		177 (6.6)	132 (6.1)	
Born in Europe (not Nordic countries)	648 (7.1)	521 (6.9)		283 (10.7)	228 (10.5)	
Born outside of Europe	719 (7.8)	555 (7.4)		309 (11.6)	245 (11.3)	
Employment status, n (%)			0.88			0.94
Unskilled workers	2242 (24.5)	1836 (27.9)		754 (35.9)	634 (36.5)	
Skilled workers	1574 (17.2)	1315 (20.0)		451 (21.5)	360 (20.7)	
Assistant non-manual employees	946 (10.3)	791 (12.0)		231 (11.0)	205 (11.8)	
High / intermediate salary employees	2000 (21.8)	1699 (25.8)		320 (15.2)	264 (15.2)	
Self-employed (including farmers)	619 (6.8)	510 (7.7)		146 (6.9)	119 (6.9)	
Other employment	558 (6.1)	434 (6.6)		200 (9.5)	155 (8.9)	
Marital status, n (%)			0.03			0.20
Living with partner	5208 (56.8)	4421 (58.6)		1176 (44.4)	1003 (46.3)	
Living alone	3949 (43.1)	3125 (41.4)		1473 (55.6)	1165 (53.7)	
Education attainment, n (%)			0.33			0.90
Under 10 years (compulsory school only)	2542 (27.7)	2033 (27.2)		874 (33.4)	703 (32.8)	
10-12 years (Upper school)	4449 (48.5)	3681 (49.2)		1336 (51.1)	1100 (51.3)	
Over 12 years (college/university level)	2067 (22.6)	1765 (23.6)		404 (15.5)	341 (15.9)	
Household adjusted income, n (%)			0.001			0.24
Low	1831 (20.0)	1342 (17.8)		784 (29.6)	587 (27.1)	
Medium-low	1833 (20.0)	1462 (19.4)		560 (21.1)	447 (20.6)	
Medium	1830 (20.0)	1526 (20.0)		539 (20.3)	452 (20.8)	
Medium-high	1829 (20.0)	1620 (21.5)		426 (16.1)	382 (17.6)	
High	1834 (20.0)	1596 (21.2)		340 (12.8)	300 (13.8)	
Risk factors and previous diseases						
Active smoker, n (%)	2653 (28.9)	2169 (29.4)	0.76	N/A	N/A	

SBP, mmHg	150.3±27.9	150.9±27.5	0.19	146±28.8	146.6±28.9	0.88
DBP, mmHg	88.0±16.4	88.3±16.3	0.29	87.7±17.2	87.7±17.2	0.91
Prior history of hypertension, n (%)	4429 (48.3)	3551 (47.1)	0.25	1107 (41.8)	898 (41.5)	0.95
LDL-C, mmol/L	3.0±1.1	3.0±1.1	0.30	3.1±1.1	3.1±1.1	0.45
Prior history of CVD	2522 (27.5)	1844 (24.5)	<0.01	612 (23.1)	443 (20.5)	0.03
HbA1c	39 (36, 47)	39 (36, 46)	0.33	40 (36. 46)	40 (36, 45)	0.50
Prior history of DM, n (%)	2216 (24.2)	1670 (22.1)	<0.01	560 (21.1)	424 (19.5)	0.01
BMI, kg/m2	28.0±4.7	28.0±4.6	0.99	27.5±4.9	27.6±4.8	0.89
Type of myocardial infarction, n (%)			0.05			0.27
STEMI	3442 (37.6)	2949 (39.1)		1235 (46.6)	1044 (48.1)	
NON-STEMI	5723 (62.4)	4600 (60.9)		1418 (53.4)	1125 (51.4)	
LVEF during admission, n (%)			0.20			0.86
Normal (≥50%)	5288 (57.7)	4476 (59.0)		1503 (63.0)	1254 (64.1)	
Mildly decreased (40-49%)	1695 (18.5)	1418 (18.7)		485 (20.3)	397 (20.3)	
Moderately - severely decreased (≤39%)	1093 (11.9)	846 (11.2)		373 (14.1)	289 (13.3)	
Medication at discharge, n (%)						
Platelet inhibitors[a]	9056 (98.8)	7487 (99.2)	0.06	2626 (99.1)	2157 (99.4)	0.12
Lipid-lowering agents[b]	8881 (96.9)	7398 (97.9)	<0.01	2599 (98.0)	2134 (98.4)	0.37
ACEi or ARB	7767 (84.7)	6472 (85.8)	0.10	2233 (84.2)	1841 (84.9)	0.51
B-blockers	8214 (89.6)	6784 (89.9)	0.90	2405 (90.7)	1971 (90.9)	0.86

Results are presented as numbers and percentages (%), means±SD or medians (q1, q3). P-values are presented as * Patients with index MI vs. Patients with a one-year follow-up and ** Active smokers with index MI vs. Active smokers at baseline with a one-year follow-up.
MI, myocardial infarction; SBP, systolic blood pressure; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; CVD, cardiovascular disease; HbA1c, Haemoglobin A1c; DM, diabetes mellitus, BMI, body mass index; STEMI, ST-elevation myocardial infarction; LVEF, left ventricular ejection fraction; ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin-II receptor blocker.
[a]Platelet inhibitors included acetylsalicylic acid, clopidogrel, ticlopidine, prasugrel, ticagrelor or other platelet inhibitors.
[b]Lipid-lowering agents included statins, ezetimibe, fibrates or other lipid-lowering agents.

Organizational and patient-level predictors of risk factor outcomes

Results from the OPLS-DA are displayed in Figures 21, 22 and 23. Positive predictors are displayed first and divided into Organizational predictors (dark blue) and Patient-level predictors (light blue). Organizational predictors are further grouped into *In-hospital work routines*, *The cardiac rehabilitation team and facilities*, *Structure of the cardiac rehabilitation programme*, and *exCR*. Negative predictors from all groups are shown at the bottom of each diagram (red). Exact VIP (±SE) and loading values (±SE) for all variables with VIP >0.8 and CI not including zero are listed in Supplementary materials 4-6.

Out of the 71 organizational variables included in the analysis 36 were identified as meaningful predictors for reaching target outcomes LDL-cholesterol and 35 for BP at one-year post-MI.

For both LDL-cholesterol and BP, a few variables from *In-hospital work routines* were identified as meaningful (indicated with VIP±SE for LDL-cholesterol and BP). They included having written discharge consult protocols for the physician responsible for the patient discharge (1.7±0.3 and1.6±0.4) and providing the patient with written information on risk factors (1.0±0.4 and 1.4±0.4) and lifestyle (0.8±0.2 and 1.2±0.4).

For both LDL-cholesterol and BP, meaningful variables from *The cardiac rehabilitation team and facilities* included having a medical director (1.7±0.3 and 1.5±0.4), reporting adequate facilities (1.6±0.5 and 2.0±0.3), nurses using protocols for medication adjustment (1.6±0.2 and 1.6±0.5), having operational team meetings to discuss organizational matters and quality control (1.4±0.3 and 1.3±0.4), using audit data for quality improvement (1.0±0.2 and 1.3±0.3), and the team reporting good team spirit (1.2±0.4 and 1.2±0.3). Including a psychologist in the cardiac rehabilitation team was also of importance for both outcomes (1.6±0.3 and 2.0±0.6).

For *Structure of the cardiac rehabilitation programme* the strongest predictor for both LDL-cholesterol and BP was offering psychosocial management at the initial assessment with a nurse (2.1±0.4 and 2.3±0.4) and having extended opening hours at the cardiac rehabilitation centre (2.2±0.2 and 1.5±0.5). Other meaningful variables included cardiac rehabilitation centre coverage (the number of patients attending one-year follow-up/number of patients eligible for follow-up) (1.7±0.2 and 1.8±0.2), continuity in nurse-patient care (1.8±0.3 and 1.3±0.4) and that the need for a physician consult was adapted to patient needs (1.7±0.3 and 1.0±0.5).

The strongest predictors from the *exCR* variables for both outcomes were offering an initial pre exCR assessment with a physiotherapist (1.5±0.3 and 1.5±0.5), performing a symptom-limited exercise test at the pre exCR assessment (1.8±0.5 and 1.9±0.6), providing patients with an exercise log to register their physical activity and exercise activities at the pre exCR assessment (1.4±0.4 and 1.2±0.5), and providing different forms of exercise training modalities (1.3±0.7 and 1.8±0.3).

Low LDL-cholesterol at baseline was the strongest *Patient-level predictor* for reaching LDL-cholesterol target outcome (3.9±0.7). Likewise, not having a prior diagnosis of hypertension (2.9±0.2) and low baseline SBP (1.4±0.3) were strong predictors of reaching the BP target outcome. Second to these, participating in exCR was the strongest patient-level predictor for both outcomes (1.6±0.8 and 1.5±0.4).

For smoking abstinence, only 5 out of 71 organizational variables were identified as meaningful, the strongest was prescription of varenicline by the centre´s physicians (2.0±1.9). The strongest *patient-level predictor* for smoking abstinence was participation in exCR (2.5±0.3), followed by having no prior history of CVD (2.1±0.3), and having participated in interactive group-based patient education as a part of the cardiac rehabilitation programme (2.0±0.3). Other positive predictors included favourable socioeconomic status e.g., disposable income (1.6±0.4), living with partner (1.5±0.6) and education (0.8±0.3).

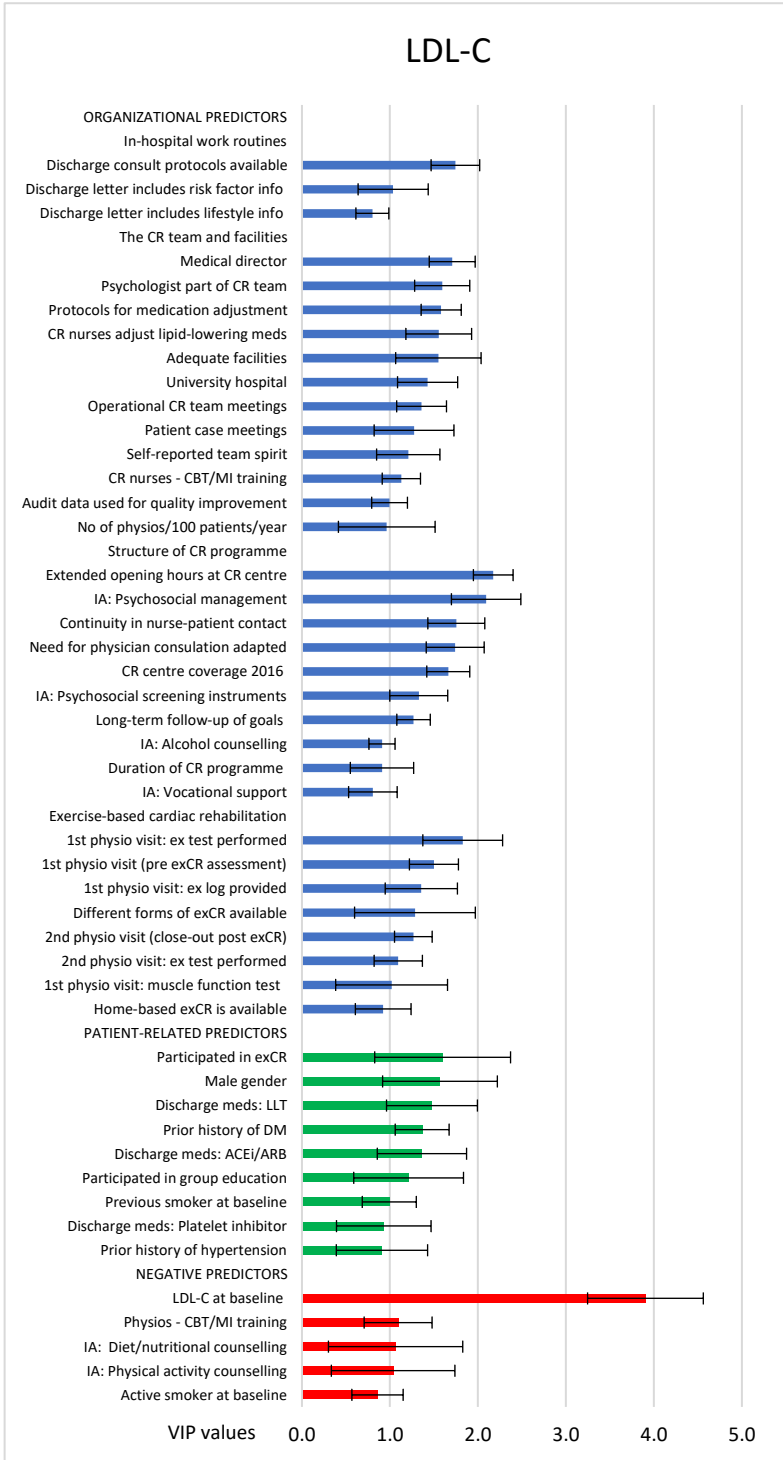

Figure 21. A bar-chart showing the results of the OPLS-DA for LDL-cholesterol.

Positive organizational (dark blue) and patient-level (green) predictors of reaching treatment targets for LDL-C (<1.8 mmol/L) at one-year after myocardial infarction. Negative predictors are shown in red. Only variables with VIP values (diplayed on X-axis) >0.8 and confidence intervals not including zero are displayed.

LDL-C, low-density lipoprotein cholesterol; CR, cardiac rehabilitation; CBT, cognitive behavioural therapy; MI, motivational interviewing, IA, initial assessment; No, number; physio, physiotherapist; ex, exercise, exCR, exercise-based cardiac rehabilitation; LLT, lipid-lowering treatment (statins, ezetimibe, fibrates or other LLT), DM, diabetes mellitus; ACEi, angiotensin converting enzyme inhibitors; ARB, angiotensin II receptor blockers.

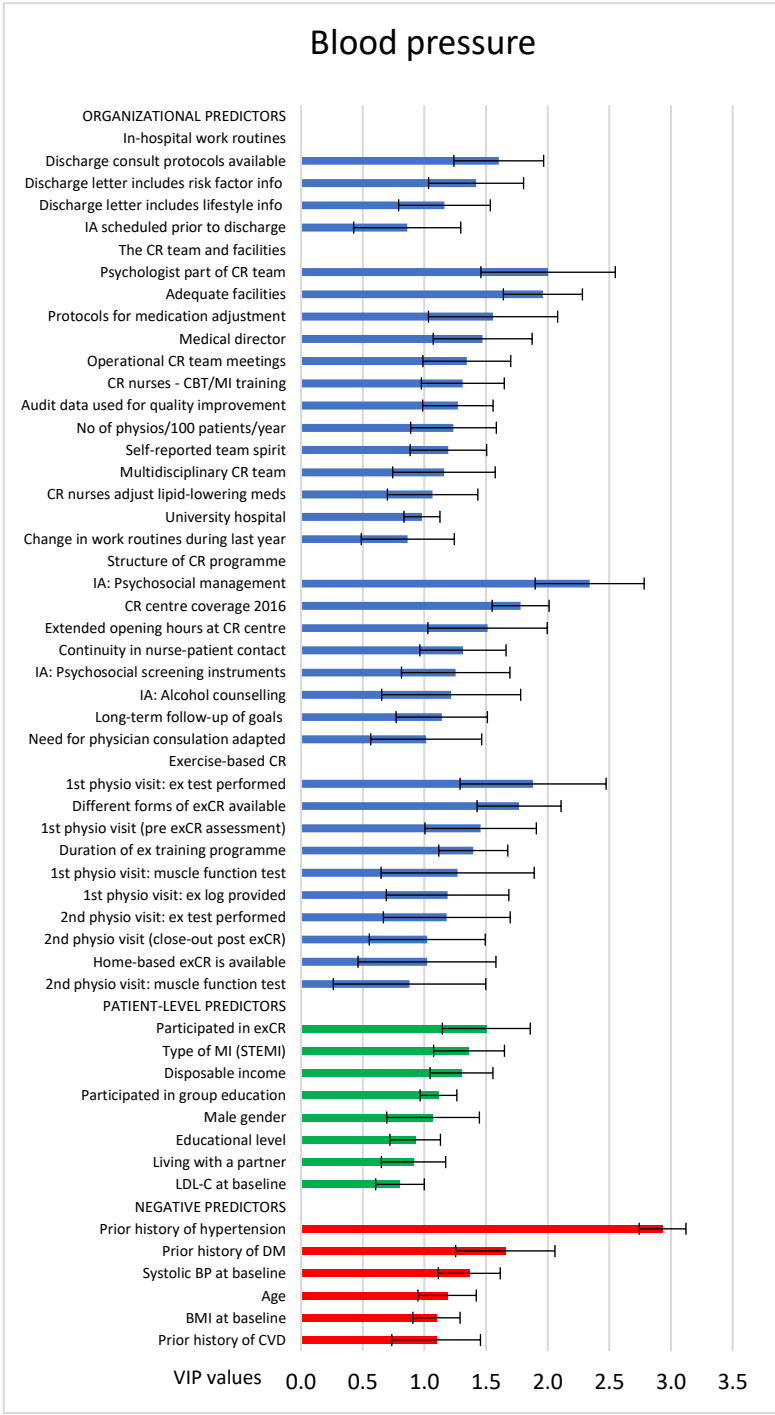

Figure 22. A bar-chart showing the results of the OPLS-DA for blood pressure.

Positive organizational (dark blue) and patient-level (green) predictors of reaching treatment targets for blood pressure (<140/90) at one-year after myocardial infarction. Negative predictors are shown in red. Only variables with VIP values (diplayed on X-axis) >0.8 and confidence intervals not including zero are displayed.

IA, initial assessment; CR, cardiac rehabilitation; CBT, cognitive behavioural therapy; MI, motivational interviewing; No, number; physio, physiotherapist; ex, exercise, exCR, exercise-based cardiac rehabilitation; MI, myocardial infarction; STEMI, ST-elevation MI; LDL-C, low-density lipoprotein cholesterol; DM, diabetes mellitus; BP, blood pressure; BMI, body mass index; CVD, cardiovascular disease.

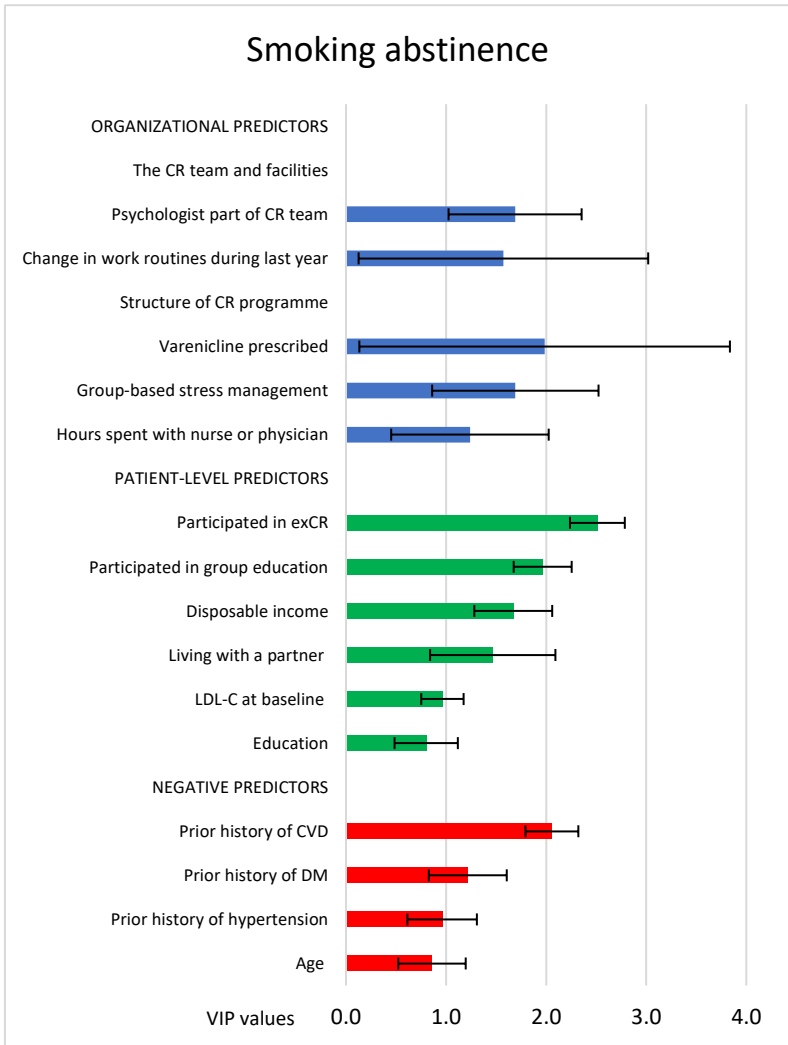

Figure 23. A bar chart showing the results of the OPLS-DA for smoking abstinence.

Positive organizational (dark blue) and patient-level (green) predictors of being abstinent from smoking at one-year post-MI. Negative predictors are shown in red. Only variables with VIP values (diplayed on X-axis) >0.8 and confidence intervals not including zero are displayed.

CR, cardiac rehabilitation; exCR, exercise-based CR; LDL-C, low-density lipoprotein cholesterol; CVD, cardiovascular disease; DM, diabetes mellitus.

Discussion

This thesis focuses on the care of post-MI patients taking part in cardiac rehabilitation. According to European guidelines, cardiac rehabilitation should be offered to patients with several different cardiac diagnoses (74). In Sweden participation is most often offered to post-MI patients and the studies in this thesis have focused on this group.

The positive effects of cardiac rehabilitation after suffering an MI are well documented (75, 76, 87), but so is the issue of its underutilization (101, 102). This thesis presents four studies that aimed to investigate cardiac rehabilitation on both a local and national level and to improve patient attainment of therapeutic goals after participating in a cardiac rehabilitation programme.

The studies approach cardiac rehabilitation from different angels. **Paper I** and **III** aimed to evaluate new methods for patient care to improve outcomes after participating in centre-based cardiac rehabilitation. These two papers present studies of a more practical nature as they explore new work routines within cardiac rehabilitation that are relatively easy to apply in clinical practice. **Papers II** and **IV** are national studies describing services in current practice provided at cardiac rehabilitation centres in Sweden and, furthermore, evaluating which services may predict patient attainment of secondary preventive therapeutic goals. As such, **Papers II** and **IV** are more general and informative, laying groundwork for future research.

Each paper will be discussed separately but reflecting on the gaps in evidence presented by the European guidelines of preventive cardiology discussed in the introduction of this thesis (18), with the studies presented here, I and my co-authors hope to contribute to filling the gaps. With **Papers I**, **III** and **IV** we aimed to improve cardiac rehabilitations programmes, trying to move closer to finding the optimal cardiac rehabilitation programme in the era or modern cardiology. In **Paper IV** we tried to add evidence on the incremental benefits of different components of cardiac rehabilitation. **Paper I** and **III** are studies of alternative models of cardiac rehabilitation. Lastly, **Papers II** and **IV** may provide a potential aid for decision making, on allocation of resources and prioritizing programme components within cardiac rehabilitation.

Main findings and significance

Paper I

In this single-centre observational study we measured several secondary preventive therapeutic goals in post-MI patients after participating in a cardiac rehabilitation programme. The study showed significantly better risk factor control of SBP, LDL- and total cholesterol in favour of tailored, nurse-led care between the first and second follow-up visits, compared to traditional care. Also, active smokers who took part in the tailored, nurse-led care reported abstinence to a higher degree than those who took part in traditional care. Our results indicate that tailored, nurse-led cardiac rehabilitation may lead to better risk factor control. Adequate risk factor control is the cornerstone of secondary prevention to prevent future coronary events (18, 76, 84). On this note, there was a trend in the number of readmissions due to cardiovascular causes in favour of the tailored, nurse-led group. During the follow-up period 3.6% patients in tailored, nurse-led group and 9.5% in the traditional care group were readmitted to hospital. But, unlike the traditional care group all readmissions in the tailored, nurse-led group were due to angina and no patients were readmitted due to acute MI, heart failure or stroke, whereas in the traditional group most readmissions were due acute MI, heart failure or stroke.

The decision of having the cardiac rehabilitation programme coordinated by nurses was based on evidence that nurse-led programmes can improve lifestyle and risk factor control (113, 114). For example, Wood *et al* published the results of the EUROACTION trial in 2008. It was a cluster-randomised, controlled trial performed in eight European countries and included over 5000 CVD- or at-risk patients. They compared a 16-week individually adjusted intervention with education sessions and motivational interviews including spouses and/or family members, with usual care. The intervention resulted in reduced risk of CVD through lifestyle changes made by families, such as adopting a healthier diet and increased physical activity (114). Nurse-led healthcare programmes have also been successful in other areas of medicine, such as the complex field of oncology, where studies have demonstrated that nurse-led programmes could benefit both patients and healthcare facilities (145). Our study supports adopting nurse-led care in cardiac rehabilitation programmes.

Our results also support individually tailored patient care, such as doing individual assessments as to which patients need cardiologist consultations and doing repeated checks of lab-values. Several changes to work routines were made compared to traditional care (Table 3). The changes in work routines that were measurable were quantified and reported. The number of follow-up visits with a cardiologist decreased significantly in the tailored nurse-led group, whilst the number of follow-up visits with a nurse remained the same. The number of telephone contacts to the

cardiac rehabilitation centre was higher in the tailored nurse-led care. These observations indicate that the risk factor outcomes can be improved with relatively simple measures, that do not require a major increase in resources or costs. Individually tailored care is advocated by guidelines and supported by studies (74, 75, 84). However, studies have been heterogenous in design and outcome measures (84). In future studies, the use of individualized change score has been suggested to be able to structurally assess individually tailored, multicomponent treatment interventions (146).

Paper II

The study was a survey-based inventory of cardiac rehabilitation services in Sweden. The study showed that, compared to our European counterparts, the overall quality of services provided at Swedish cardiac rehabilitation centres was high (147).

Well-developed parts included most centres having the recommended core professions (cardiologist, nurse, and physiotherapist) in their teams. Having multidisciplinary in-hospital teams has been reported to have clear benefits both for patients and staff in hospital wards, emergency rooms, intensive care units and operating rooms, such as to limit adverse events, improve patient outcomes and lead to both patient and staff satisfaction (148). Thus, it was positive to see that this has been made a priority within cardiac rehabilitation in Sweden. It was also relatively common that nurses independently adjusted medication. Nurse management with medication adjustment has been shown to be effective in improving patient outcomes in other chronic conditions, such as DM (149). Swift programme initiation was yet another well-developed part of Swedish cardiac rehabilitation programmes. This is important because patient adherence to secondary preventive treatments tends to decline after hospital discharge and effects of early risk factor management have been shown to reduce rates of repeated cardiovascular events and all-cause mortality (77, 150). The exCR programmes commonly offered an individual assessment with a physiotherapist and centre-based exercise training. As discussed previously, exCR has been shown in multiple studies to be a pivotal part of a comprehensive cardiac rehabilitation (87) and should be made a priority when organizing the programmes (74, 86). Finally, over half of the centres reported using SWEDEHEART data regularly for quality control. Audit and subsequent feedback to healthcare professionals has been repeatedly shown to have a positive effect professional practice (151).

The results did show that there was a variation between centres regarding which services were provided, and this was clearly displayed by the Perfect-CR index (Figure 14). In general, the study lifted some less well-developed parts of cardiac rehabilitation, for example, having regular multidisciplinary team meetings to discuss patient cases. Having multidisciplinary team meetings is well-established in

other areas of medicine and has been shown to have several positive effects, such as strengthening teamwork and shared clinical decision making (152). There was a great variation in the duration of the cardiac rehabilitation programmes. The number of staff per patient varied. Offering group education adapted to specific patient needs was lacking. The content of the initial outpatient assessment varied. Lastly, offering patients written information on therapeutic goals for risk factors and lifestyle changes or copies of their risk factor values (BP, blood test results, etc.) in writing was uncommon. Standardising patient follow-up to include all cardiovascular risk factors may improve patient outcomes (84). Lastly, handing out written information may be of importance, especially for patients with low health literacy (153, 154). In Sweden, the issue of unequal healthcare has been discussed in recent years, i.e., that patient services in different parts of Sweden vary widely (155). Our results support the need for this discussion.

Paper II was the first of its kind within Swedish cardiac rehabilitation. It gave a description of what services are provided at cardiac rehabilitation centres, providing us with an idea of where we stand on an international level and, also how level of service differs between different centres. Doing a regular inventory of services provided across the county could be beneficial to both those organizing healthcare and to patients. This is performed, for example, in the United Kingdom (UK), where the National Audit of Cardiac Rehabilitation (NACR) audits a set of six minimum standards that cardiac rehabilitation centres should meet and the results are published annually (156). The reports illustrate if the UK programmes are following recommendations and if services are improving over time. It may benefit patients in a way that it may decrease inequalities between centres, as it should not make a difference where one suffers an MI.

After the publication of Paper II, the participating cardiac rehabilitation centres have been offered written reports on their own results, which were compared to results from rest of the country. Also, several workshops have been conducted for cardiac rehabilitation staff that included lectures and groupwork with the aim to learn from colleges for programme improvement. Furthermore, the results have contributed to the development of a national strategy document aiming to decrease the differences in services provided at cardiac rehabilitation centres by providing national standards of care. Lastly, the paper has led to the implementation of variables reflecting cardiac rehabilitation structure and content in the SWEDEHEART registry.

Paper III

The primary outcome in this study was change in submaximal exercise capacity during two separate physiotherapy visits. While attendance to physiotherapy visits was high only 69% of the patients in the intervention group and 83% in the usual care group completed the submaximal exercise-tests at both visits and were included in the analysis. The results showed that both the intervention group and the usual

care group improved their exercise capacity between the first and second exercise test. Between the groups there was a difference of 4.1W in exercise-capacity favouring the intervention group, the difference was however, non-significant. Using telehealth as an adjunct to comprehensive cardiac rehabilitation has demonstrated increased physical activity levels in previous studies (157, 158). In our study the web-based application did not specifically promote adherence to the exCR programme, but rather to increase physical activity levels in general, which may, perhaps, explain the lack of a larger difference in exercise capacity between groups.

On the other hand, the intervention group had favourable outcomes when it came to BP. In the unadjusted analysis, patients in the intervention group had decreased their SBP significantly more at the 2-week follow-up than the usual care group. After adjusting for relevant covariates, the observed differences in BP increased, in favour of the intervention group, and included a significant difference in SBP and DBP at the 6-10-week follow-up. A numerical but non-significant difference in BP between groups remained throughout the trial period. An improvement in reaching BP goals when having access to a web-based application when taking part in cardiac rehabilitation is in line with previous studies (159-161). Since intake of medication was the most reported parameter in the web-application (Figure 18) one possible reason for improved BP values in the intervention group might have been increased adherence to antihypertensive medication (158, 162).

Our results also demonstrated an initial beneficial effect on dietary choices in favour of the intervention group, mostly due to an increase in the consumption of fish and fruit. There were no significant differences in reported for diet the rest of the follow-up period. Previous studies on eHealth in cardiac rehabilitation have had mixed results, both showing improvement and no effect on dietary habits (119, 157, 160). Our results are based on self-reported data registered at the three occasions and not on information patients logged into the web-application in real time. Self-reported measurements have some limitations including recall bias and social desirability bias and should be interpreted with caution. All in all, it remains unclear if eHealth as a complement to comprehensive cardiac rehabilitation benefits patients with regards to diet.

There was a numerical trend towards increased smoking cessation in the intervention group throughout the trial period. The number of smokers in the study was however low and the differences non-significant. Whether the numerical difference was due to the intervention or a chance finding cannot be stated. As for diet, effect of eHealth interventions in cardiac rehabilitation on smoking cessation have shown mixed results (157, 158). And again, the data was self-reported leaving the possibility of the before mentioned biases. Current European recommendations on smoking cessation include face-to-face interventions by healthcare professionals combining therapeutic education, behavioural support and pharmacotherapy (163). The role of eHealth in smoking cessation is still unclear. To be able to better evaluate

the role of eHealth for smoking cessation one might take into consideration the European recommendations that specify certain criteria for assessment of smoking cessation in scientific work. The criteria for smoking cessation include, for example a set minimum of 6-month duration to be defined as smoke-free and having bio-chemical validation (163).

While uptake to the web-based application was high, adherence declined over time. In 2016 Buys *et al* reported a general interest in technology-enabled home-based cardiac rehabilitation among patients with CVD. Their study demonstrated that patient with different characteristics were interested in different types of technology-based cardiac rehabilitation, for example, that older patients were more interested in web-based options and younger patients were more interested in application-based options. This indicates that patient characteristics is one possible determining factor for whether the use of eHealth in cardiac rehabilitation can be successful. Buys *et al* also looked at what aspects of patients taking part in cardiac rehabilitation were most interested in having in a technology-based platform; these were ideas on exercise, healthy meals, and stress management (164). This indicates that even if technology-based cardiac rehabilitation aims to make traditional cardiac rehabilitation more flexible and individualized, the technology platforms probably need to be adjusted to individual need for optimum effect.

eHealth opens an array of new ways to optimize the use of otherwise limited healthcare resources and to add flexibility to rigid follow-up structures. eHealth interventions also have the potential to reach a large part of the population, overcoming for example distance and communication barriers (118). In Europe, internet access is high (165) and while older adults are less likely than younger adults to use mobile technology, recent trends have shown significant increases in internet use by older adults (166). Thus, age is becoming less of a barrier of use of eHealth in healthcare. The use of home-based healthcare has been especially relevant during the last year with the Covid-19 pandemic, when for example, in the UK, participation in group-based cardiac rehabilitation decreased by 36% and the use of home-based cardiac rehabilitation increased by 16% (156). The same trends were seen within Swedish cardiac rehabilitation, with fewer physical follow-ups and more follow-ups via telephone (46). Hence, our study and others alike are highly relevant.

We accept that the results of our primary outcome were not statistically significant. We speculated as to if it may have been due to missing data, however, applying retrospective sample size calculations using the planned sample size (50:100) and the observed difference of 4.1 W confirmed that statistically significant results would not have been attained, for this we would have needed a bigger sample size. With the results at hand, we can conclude that the web-based application may be a beneficial tool for certain patients taking part in cardiac rehabilitation, primarily effecting BP and diet. Attrition rates, however, indicate that it does not suit everyone. More studies are needed, focusing on developing applications to patients

liking to overcome user attrition, and perhaps testing one application feature at a time, to see which application features has effect on which lifestyle change.

Paper IV

This study was a registry- and survey-based study using data from national registries aiming to identify predictors of reaching therapeutic goals for LDL-cholesterol, BP, and smoking cessation.

About half of the organizational variables included in the analysis were identified as meaningful predictors for reaching LDL-cholesterol and BP outcome targets at one-year post-MI. The strongest predictors were mostly from on the variable groups; *The cardiac rehabilitation team and facilities, Cardiac rehabilitation programme structure* and *ExCR*. The predictors included offering psychosocial management, having a psychologist in the cardiac rehabilitation team, having extended opening hours, the staff reporting adequate facilities, having a medical director, nurses using protocols for medication adjustment, having team meetings to discuss organizational matters, using audit data for quality improvement and the team reporting good team spirit. Thus, our results support providing structure and management, a multidisciplinary team, educated autonomic staff and a good work environment, all of which have been shown to positively effect patient care (167-171). Interestingly, the majority of the *exCR* variables included in the analysis were identified as meaningful. Studies have shown that participation in exCR reduces cardiovascular mortality, improves key risk factors (cholesterol, SBP and smoking) and reduces hospital readmissions (87, 171). Our results add to the bulk of evidence supporting the importance of exCR. It was also interesting to see that many organizational variables predicted LDL-cholesterol and BP goal attainment. As organizational variables can be influenced by staff, management, and policy providers, this brings hope that there is room for improvement in LDL-cholesterol and BP goal attainment in the future not only by introducing new types of therapy but also by making better use of currently available work methods and resources.

When it came to *Patient-level predictors* having low LDL-cholesterol at baseline was the strongest predictor of being at target for LDL-cholesterol at one-year and, likewise, having no prior history of hypertension was the strongest predictor of reaching BP targets. These results were not surprising. They do underline the importance of adequate treatment of risk factors as a part of primary CVD prevention (18, 172).

Also, participation in exCR was a strong positive patient-level predictor for reaching both LDL-cholesterol and BP, further underlining the importance of exCR. However, this may be influenced by selection bias since patients participating in exCR may be more motivated to lifestyle changes and medication compliance and, thus, be more prone to reach therapeutic goals.

The outcome variable for smoking cessation was self-reported, having limitations that have previously been discussed. For smoking cessation, *Patient-level variables* were predominant predictors. Only five organizational variables were identified as meaningful, and all were parts of the groups: *Cardiac rehabilitation team and facilities,* and *Cardiac rehabilitation programme structure.* The strongest one was varenicline being prescribed by the centre´s physicians. Previous studies have shown that varenicline can significantly increase the likelihood of achieving smoking cessation, however the treatment is highly underutilized within cardiac rehabilitation (102, 173). Our results underline that physicians should more actively prescribe varenicline to aid in smoking cessation.

One organizational variable predicting smoking cessation was also a strong predictor of reaching therapeutic goals for LDL-cholesterol and BP, this was having a psychologist or social worker as part of the cardiac rehabilitation team. There is substantial evidence behind the importance of psychosocial risk factors and cardiovascular health and prognosis, but there is less evidence regarding indications, screening methods or of the value of therapeutic interventions and their impact on prognosis (174). Having a psychologist in the cardiac rehabilitation teams is recommended (74). Also recommended is having individual counselling sessions with a psychologist for patients to share concerns and receive tailored education. Educational interventions can affect a patient's psychological state positively and reduce misconceptions about CVD and its outcomes (174). In our study, having a psychologist or social worker as a part of the cardiac rehabilitation team might also reflect centres that have well-functioning multidisciplinary organizations.

Hours spent with a nurse or physician was a positive predictor of smoking cessation, indicating that smokers perhaps need a more intensive face-to-face programme than non-smokers. Supporting this idea, was also the variable that group-based stress management was offered at the centre, which was a positive predictor of smoking cessation. On the patient-level side participation in group education and participation in exCR, both requiring physical contact with the patient, were positive predictors. This should, however, be interpreted with caution as it may be influenced by selection bias.

Variables indicating a favourable socioeconomic status were positive predictors for smoking cessation while age and prior disease history were negative predictors, all attributes not modifiable by the cardiac rehabilitation team. The same predictors have in previous studies been identified as predictors for attendance in cardiac rehabilitation (175). The results might indicate that smokers are a more vulnerable patient group and may need more individually adjusted programmes compared to non-smokers.

Paper IV was an observational predictive study providing information on which programme- and patient-level characteristics could predict patient achievement of therapeutic goals. Previous studies on cardiac rehabilitation have tried to find clues

to achieving better outcomes of cardiac rehabilitation through interventional studies (176, 177). Despite the many published studies, some of the recommendations on the structure of cardiac rehabilitation programmes in the European guidelines are not based in clinical evidence (74, 75). Our study is, to our knowledge, the first of its kind. It is a piece of the puzzle in building up the evidence behind effective cardiac rehabilitation programmes. However, one should keep in mind the crudeness of the statistical method. Rather than focusing on each variable´s potential effect one should take a step back and focus on patterns. Also, one should keep in mind that certain programme characteristics instead of being very important on their own are perhaps proxies for well-functioning ambitious cardiac rehabilitation programmes. The results should be built on, first, by confirming the results with other statistical methods and, second, by doing trials in a controlled setting, both of which are underway.

Strengths and limitations

An overall strength of this thesis is the difference in study design and statistical methods. The aims of the studies were to add data to gaps in current evidence, making them relevant for current clinical practice. The studies included in this thesis used well-established nationwide registries.

The biggest limitation in **Paper I** was that multiple changes were implemented and tested at the same time making it difficult to draw a conclusion as to which change, or new work routine led to which result. However, an advantage was that the changes in follow-up structure were simple and of low cost and should thus be easy to replicate at other cardiac rehabilitation centres.

The biggest strength of **Paper II** was the high participation in the study, with a 100% response rate. Limitations included that answers were self-reported, and that the questionnaire was not validated, both of which may impact the validity and reliability of the results.

The study in **Paper III** benefitted from SWEDEHEART´s prespecified time-points for follow-up and procedures which provided a standardization that otherwise could be a challenge in multicentre trials. One limitation was that the study was unblinded. Blinding is, however, a challenge in eHealth trials. Also, the follow-up data did not include information on the use of commercial eHealth applications by the patients in the usual care group.

The statistical method (OPLS-DA) used in the study in **Paper IV** had both strengths and limitations. One advantage is being able to analyse large numbers of variables, allowing us to look for patterns in prediction and investigate relations between all variables in a single context. As cardiac rehabilitation is a multifaceted treatment with multiple interlinked interventions the OPLS-DA has clear advantages over more traditional regression analyses which are sensitive to collinearity. However, a major limitation was the coarseness of the data analysis.

Conclusions

Paper I

Providing a tailored, nurse-led cardiac rehabilitation programme may benefit post-MI patients by improving risk factor management specifically for SBP, LDL- and total cholesterol and smoking, all factors that decreases the likelihood for future coronary events. Future studies on individualized care should use standardized methods to structurally assess individually tailored, multicomponent treatment interventions.

Paper II

The overall quality of cardiac rehabilitation services provided in Sweden is high with many of the European recommendations being followed in clinical practice. There were, however, observed differences in services provided between centres and some recommendations were less often followed, compared to others. These included having structured teamwork including regular team meetings, standardizing patient follow-up including all cardiovascular risk factors, and regularly using registry data with the aim to improve work routines.

Paper III

Our results add to existing evidence suggesting that complementing comprehensive cardiac rehabilitation programmes with a web-based application may positively affect patient risk factor outcomes and lifestyle, including BP and dietary choices. More studies are needed using methods to overcome user attrition, and more closely investigate which application features have effect on which lifestyle change.

Paper IV

The study identified multiple organizational and patient-level predictors for reaching key risk factor targets one-year post-MI. The results might contribute to defining the optimal composition of comprehensive cardiac rehabilitation programmes.

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Supplementary material

Supplementary material 1

Kära SEPHIA vänner!

Tack för att Ni tar Er tid för att svara på denna enkätstudie. Syftet med enkäten är att kartlägga strukturer och arbetsrutiner inom svensk hjärtrehabilitering och analysera hur dessa är kopplade till måluppfyllelse i SEPHIA, följsamhet till läkemedelsbehandling och återinsjuknande efter hjärtinfarkt.

Om inte annat specificeras, vänligen svara utifrån hur Er verksamhet har sett ut under 2016.

Välj de svarsalternativ som bäst beskriver den dagliga verksamheten.

Vi har samlat frågor som berör sjukgymnastik och träning till sista kapitlet, varför vi rekommenderar att Era sjukgymnaster/fysioterapeuter är närvarande när detta kapitel besvaras.

Några definitioner:

Hjärtrehabilitering: Ett strukturerat uppföljnings- och behandlingsprogram, lett av ett multiprofessionellt team.

Programmet bör innehålla följande:

- Individualiserad bedömning och uppföljning av patienten
- Behandling av kardiovaskulära riskfaktorer
- Deltagande i patientutbildning (enskilt och/eller i grupp)
- Sjukgymnast-/fysioterapeut-ledd träning

Hjärtrehabiliteringsenhet: Öppenvårdsverksamhet som bedriver hjärtrehabilitering enligt ovan.

Med hjärtrehabilitering menas sjukhusbaserad hjärtrehabilitering (dvs. ej hembaserad hjärtrehabilitering), om inte annat specificeras.

TACK för Er medverkan!

Bakgrundsinformation och faciliteter

Namnet på Er enhet:

_____

Adressen till Er enhet:

_____

Följande frågor avser lokaler för hjärtrehabiliteringsverksamheten.

Vi har tillfredsställande mottagningslokaler för enskilda patientbesök till sjuksköterska.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Vi har tillfredsställande mottagningslokaler för enskilda patientbesök till läkare.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Vi har tillfredsställande lokaler för gruppundervisning (ex hjärtskola):

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Patienterna

Frågorna i Perfect-CR enkäten avser patienter som drabbats av hjärtinfarkt. Inledningsvis ber vi Er dock svara mer övergripande på vilka patienter erbjuds hjärtrehabilitering på Er enhet.

Deltagande i hjärtrehabilitering erbjuds följande patienter med hjärtsjukdom (markera alla alternativ som stämmer):

□ Patienter som vårdats för hjärtinfarkt

□ Patienter som vårdats för instabil angina

□ Patienter som vårdats för stabil angina

□ Patienter som har genomgått elektiv CABG

□ Patienter som har genomgått elektiv PCI

□ Stabil kranskärlssjukdom (utan föregående akut händelse, elektiv PCI eller CABG)

□ Patienter med hög risk för kranskärlssjukdom (ex patienter med diabetes, metabola syndromet eller familjär hyperkolesterolemi)

☐ Patienter med hjärtsvikt

☐ Patienter med hjärtarytmier

☐ Patienter som fått pacemaker eller ICD

☐ GUCH patienter

☐ Patienter som genomgått övrig hjärtkirurgi än CABG

☐ Patienter som genomgått hjärttransplantation

☐ Patienter med perifer kärlsjukdom

☐ Andra: _____

Härefter avser frågorna endast patienter som drabbats av hjärtinfarkt.

Patienter som drabbats av hjärtinfarkt erbjuds deltagande i hjärtrehabilitering oavsett ålder (välj ett svar).

☐ Ja

☐ Nej

☐ Vet inte

Om ni har en åldersgräns, vilken ålder (skriv om det är < eller ≤)? _____år

Enligt er uppfattning, hur stor andel av hjärtinfarktpatienter som deltar i hjärtrehabiliteringen är födda utanför Sverige (oavsett om de talar svenska eller inte)? _____%

Motsvarar detta, enligt Er uppfattning, andelen hjärtinfarktpatienter födda utanför Sverige (oavsett om de talar svenska eller inte) som vårdas för hjärtinfarkt på avdelningen (välj ett svar)?

☐ Ja, det är samma andel

☐ Nej, hjärtinfarktpatienter födda utanför Sverige är underrepresenterade på hjärtrehabiliteringsenheten

☐ Nej, hjärtinfarktpatienter födda utanför Sverige är överrepresenterade på hjärtrehabiliteringsenheten

☐ Vet ej

Hur upplever Ni att hjärtinfarktpatienter födda utanför Sverige (oavsett om de talar svenska eller inte) uppnår sekundärpreventiva behandlingsmål?

☐ Betydligt sämre än de som är födda i Sverige

□ Något sämre än de som är födda i Sverige

□ Likvärdigt

□ Något bättre än de som är födda i Sverige

□ Betydligt bättre än de som är födda i Sverige

□ Vet inte

Enligt Er uppfattning, hur stor andel av hjärtinfarktpatienter som deltar i hjärtrehabiliteringen talar inte svenska (dvs kräver tolk för samtal) ? _____%

Motsvarar detta enligt Er uppfattning andelen hjärtinfarktpatienter som inte talar svenska (dvs kräver tolk för samtal) som vårdas för hjärtinfarkt på avdelningen (välj ett svar)?

□ Ja det är samma andel

□ Nej patienter som inte talar svenska är underrepresenterade på hjärtrehabiliteringsenheten

□ Nej patienter som inte talar svenska är överrepresenterade på hjärtrehabiliteringsenheten

□ Vet ej

Hur upplever Ni att patienter som inte talar svenska (dvs kräver tolk för samtal) uppnår sekundärpreventiva behandlingsmål?

□ Betydligt sämre än de som är födda i Sverige

□ Något sämre än de som är födda i Sverige

□ Likvärdigt

□ Något bättre än de som är födda i Sverige

□ Betydligt bättre än de som är födda i Sverige

□ Vet inte

Vårdtiden och utskrivningssamtalet

Följande frågor rör patienter som har varit inneliggande på vårdavdelning på grund av hjärtinfarkt innan de remitteras till hjärtrehabiliteringsenheten.

Patienterna träffar en sjuksköterska som arbetar på hjärtrehabiliteringsenheten under vårdtiden för att diskutera uppföljningen.

Stämmer inte alls			*Stämmer helt*			*Vet inte/ Ej aktuellt*
1	2	3	4	5	6	□/□

Sjuksköterska som arbetar på hjärtrehabiliteringsenheten är med vid läkarens utskrivningssamtal.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Sjuksköterska som arbetar på hjärtrehabiliteringsenheten har ett eget utskrivningssamtal.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Det finns skriftliga instruktioner (ex PM/checklista) för läkare som avser läkarens utskrivningssamtal (välj ett svar).

□ Ja

□ Nej

□ Vet inte

Information om uppföljningens struktur (ex när patienten kallas till första besök, vilka yrkeskategorier han/hon kommer att träffa och hur länge han/hon kommer att följas upp) förmedlas till patienten vid utskrivningssamtal på följande sätt (välj ett eller flera alternativ från listan):

□ Patienten får en bokad tid till första återbesök innan hemgång

□ Skriftlig individualiserad information (ex som del av läkarens utskrivningsmeddelande eller separat papper)

□ Skriftlig allmänt hållen information (ex förtryckt papper, broschyr eller häfte)

□ Muntlig information

□ Hänvisning till egen eller extern webbsida

□ Ingen information

□ Vet inte

Information om vilka läkemedel patienten skall ta förmedlas till patienten vid utskrivningssamtal på följande sätt (välj ett eller flera alternativ från listan):

□ Skriftlig individualiserad information (ex som del av läkarens utskrivningsmeddelande eller separat papper)

□ Skriftlig allmänt hållen information (ex förtryckt papper, broschyr eller häfte)

□ Muntlig information

- Hänvisning till egen eller extern webbsida
- Ingen information
- Vet inte

Information om sekundärpreventiva behandlingsmål avseende blodtryck (<140/90 mmHg) och LDL kolesterol (<1,8 mmol/L) förmedlas till patienten vid utskrivningssamtalet på följande sätt (välj ett eller flera alternativ från listan):

- Skriftlig individualiserad information (ex som del av läkarens utskrivningsmeddelande eller separat papper)
- Skriftlig allmänt hållen information (ex förtryckt papper, broschyr eller häfte)
- Muntlig information
- Hänvisning till egen eller extern webbsida
- Ingen information
- Vet inte

Information om sekundärpreventiva behandlingsmål som avser levnadsvanor (ex vikten av rökstopp, hälsosam kosthållning, fysisk aktivitet och träning) förmedlas till patienten vid utskrivningssamtalet på följande sätt (välj ett eller flera alternativ från listan):

- Skriftlig individualiserad information (ex som del av läkarens utskrivningsmeddelande eller separat papper)
- Skriftlig allmänt hållen information (ex förtryckt papper, broschyr eller häfte)
- Muntlig information
- Hänvisning till egen eller extern webbsida
- Ingen information
- Vet inte

Om patienten erhåller skriftligt kontrakt/hälsoplan som avser den sekundärpreventiva behandlingen (ex medicinering, riskfaktorer och/eller levnadsvanor), undertecknas denna vid utskrivningssamtalet av följande (välj ett eller flera alternativ från listan):

- Patienten får inget skriftlig kontrakt/hälsoplan
- Kontrakt/hälsoplan undertecknas av vårdpersonal
- Kontrakt/hälsoplan undertecknas av patienten

□ Vet inte

Anhöriga deltar vid läkarens utskrivningssamtal.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

För patienter som inte talar svenska – vem tillåts tolka vid utskrivningssamtal (välj ett eller flera alternativ från listan)?

□ Anhöriga

□ Vårdpersonal som talar patientens språk

□ Professionell tolk

□ Vet inte

För patienter som inte talar svenska:

Markera de alternativ (ett eller fler) som bäst beskriver den sedvanliga rutinen vad gäller material som lämnas över till patienten vid utskrivningssamtal.

	Översätts till patientens språk	Översätts till engelska	Finns förtryckta på andra språk än svenska	Delas ut på svenska	Delas inte ut
Läkarens utskrivningsinformation					
Läkemedelslista					
Information om riskfaktorer och levnadsvanor					
Information om uppföljningens struktur					

Hjärtrehabiliteringsteamets sammansättning

Vilka professioner ingår i hjärtrehabiliteringsteamet? Välj det alternativ som bäst beskriver situationen för respektive yrkeskategori.

	Anställd på kliniken	Anställd på annan klinik/enhet	Ingår inte i teamet men är tillgänglig på konsultbasis	Vi har ingen
Sjuksköterska				
Sjukgymnast/fysioterapeut				
Läkare				
Psykolog				
Kurator				
Dietist				
Arbetsterapeut				
Undersköterska				
Andra: _____				

Finns det en utsedd medicinskt ansvarig läkare för hjärtrehabiliteringsenheten, annan än verksamhetschef/sektionschef (välj ett svar)?

☐ Ja

☐ Nej

☐ Vet inte

Hur många heltids sjuksköterske-tjänster (ex 1,5) finns inom/tillhör Er hjärtrehabiliteringsenhet som avser omhändertagande av patienter med hjärtinfarkt?

_____

Tjänstgör sjuksköterskorna enbart på hjärtrehabiliteringsenheten eller också på avdelningen (välj ett svar)?

☐ Tjänstgör enbart på hjärtrehabiliteringen

☐ Tjänstgör också på avdelning

☐ Vet inte

Har sjuksköterskorna genomgått vidareutbildning i kognitiv beteendeterapi och/eller motiverande samtal (MI) (minimum 2 dagars utbildning)?

Nej, ingen av dem					*Ja, alla*	*Vet inte*
1	2	3	4	5	6	☐

Hjärtrehabiliteringsteamet har regelbundna team-träffar för att diskutera verksamheten, dvs. inte ronder för att diskutera kliniska patientärenden utan möten avsedda för att diskutera arbetsrutiner, SEPHIA resultat, verksamhetsmål etc (välj ett svar).

☐ Ja, vi har team-träff en gång i veckan eller mer ofta

☐ Ja, vi har team-träff en eller två gånger i månaden

☐ Ja, vi har team-träff en eller två gånger per termin

☐ Ja, vi har team-träff någon gång om året

☐ Ja, men vi har team-träff oregelbundet

☐ Nej, vi har inga team-träffar

☐ Vet inte

Om ja, vilka deltar i team-träffar:

	I princip alltid	Ofta	Enstaka gånger	Aldrig	Vet inte	Vi har ingen
Sjuksköterska						
Sjukgymnast/fysioterapeut						
Läkare						
Psykolog						
Kurator						
Dietist						
Arbetsterapeut						
Undersköterska						
Andra: _____						

Denna fråga avser ronder där kliniska patientärenden tas upp (välj ett svar):

- ☐ Vi har regelbundna ronder flera gånger i veckan där sjuksköterskor och sjukgymnaster/fysioterapeuter kan ta upp sina kliniska frågor med läkare
- ☐ Vi har regelbundna ronder enligt ovan, en-två gånger i veckan
- ☐ Vi har regelbundna ronder enligt ovan, dock mer sällan än en gång i veckan
- ☐ Vi har inga regelbundna ronder utan tar upp frågor vid behov med läkare
- ☐ Vi har ingen möjlighet att ta upp kliniska frågor med läkare
- ☐ Vet ej

Hur skulle du skatta teamkänslan i hjärtrehabiliteringsteamet, yrkesgrupper emellan (sjuksköterskor, sjukgymnaster/fysioterapeuter, läkare etc)? Teamkänsla kan kännetecknas av flexibilitet, där medarbetarna förstår värdet av gemensamma rutiner och mål. Där nya idéer uppskattas och tas tillvara och där medarbetarna känner att de har tillräckliga befogenheter/kompetens för att kunna utföra sitt arbete på bästa sätt.

Dålig teamkänsla *Bra teamkänsla* *Vet inte*

1 2 3 4 5 6 ☐

Används data från SEPHIA (Sveriges kvalitetsregister för sekundärprevention) för kvalitetsarbete och uppföljning av verksamhetsmål inom hjärtrehabiliteringen (välj ett svar)?

- ☐ Ja, regelbundet
- ☐ Ja, ibland
- ☐ Nej
- ☐ Vet inte

Vilken personalomsättning har ni haft i hjärtrehabiliteringsteamet hos följande yrkeskategorier under den senaste 2-års perioden? Välj det alternativ som bäst beskriver situationen för respektive yrkeskategori.

	Samma personal som för 2 år sedan	Delvis ny personal	Till största del ny personal	Ingen kvar av dem som jobbade i teamet för 2 år sedan	Vet inte	Ej tillämpligt
Sjuksköterskor						
Sjukgymnaster/fysioterapeuter						
Medicinskt ansvarig läkare						

Vi har haft vakanser (dvs. icke tillsatta tjänster) för följande professioner under år 2016 (välj ett eller flera alternativ från listan):

- ☐ Sjuksköterskor
- ☐ Sjukgymnaster/fysioterapeuter
- ☐ Medicinskt ansvarig läkare
- ☐ Inga vakanser

Uppföljningens struktur och innehåll

Frågorna berör endast patienter som drabbats av hjärtinfarkt.

Hur lång tid efter utskrivning från sjukhuset sker i regel den första fysiska kontakten med patienten?

	Antal veckor	Ej tillämpligt
Till sjuksköterska		
Till sjukgymnast/fysioterapeut		
Till läkare		

Vid första sjuksköterskebesöket görs följande:

	Ja	Nej	Vet ej	Ej tillämpligt
Bedömning av patientens matvanor				
Rådgivning om matvanor				
Bedömning av patientens motions- och träningsvanor				
Rådgivning om fysisk aktivitet				
Rådgivning om fysisk träning				
Bedömning av eventuell tobakskonsumtion				
Rådgivning om rökstopp hos rökare				
Bedömning av alkoholvanor				
Rådgivning om alkoholvanor				
Mätning av blodtryck				
Justering av blodtryckssänkande behandling				
Mätning av vikt				
Mätning av midjemått				
Rådgivning om viktnedgång hos överviktiga				
Mätning av lipider eller bedömning av nivåer tagna under vårdtiden				
Justering av lipidsänkande behandling				
Mätning av fasteglukos och/eller HbA1c eller bedömning av nivåer tagna under vårdtiden				
Muntlig bedömning av psykisk ohälsa (ångest, depression och stress)				
Strukturerad bedömning av psykisk ohälsa (ångest, depression och stress) via skattningsskalor				
Rådgivning vid psykisk ohälsa, ex hänvisning till PV/kurator/psykolog				
Bedömning av patientens sociala situation (dvs. vilket stöd patienten har i sin omgivning, arbetssituation, ekonomiska bekymmer mm)				
Genomgång av aktuell läkemedelslista				
Patienten får skriftliga mål avseende riskfaktorer och levnadsvanor				
Patient får skriftlig kopia av sina värden (blodprov, blodtryck etc)				

Utförs glukosbelastning (oralt glukostoleranstest, OGTT) på patienter med hjärtinfarkt utan känd diabetesdiagnos hos Er (välj ett svar)?

- ☐ Ja, på alla patienter
- ☐ Ja, på selekterade patienter
- ☐ Nej, vi gör inte OGTT
- ☐ Vet ej

Om glukosbelastning (oralt glukostoleranstest, OGTT) utförs, när görs detta (välj ett svar)?

□ Under vårdtiden

□ Efter utskrivning

□ Vet ej

Hur handläggs patienter med nyupptäckt och/eller dysreglerad diabetes (välj ett eller flera alternativ från listan)?

□ Gemensam vårdkonferens med endokrin/diabeteskollegor på sjukhuset

□ Diabetesbehandling justeras av hjärtrehabiliteringenhetens egna läkare

□ Remiss till patientens diabetes-ansvarige läkare inom primärvård/diabetesmottagning

□ Remiss till patientens diabetes-ansvariga sjuksköterska inom primärvård/diabetesmottagning

□ Rutiner saknas

□ Vet inte

Om patienten har erhållit individualiserade riskfaktormål vid utskrivning/första besök följs dessa systematiskt upp vid uppföljande besök på hjärtrehabiliteringsenheten.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Patienterna träffar samma sjuksköterska under hela uppföljningen vid hjärtrehabiliteringsenheten.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Anhöriga uppmuntras skriftligen (i kallelse eller liknande) följa med till besöken på hjärtrehabiliteringsenheten.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Hur stor andel av patienterna uppskattar ni tar med sina anhöriga? _____%

Sjuksköterskorna på hjärtrehabiliteringsenheten titrerar upp/ner följande läkemedel:

	Titrerar upp	Titrerar ner	Nyinsätter	Gör inga ändringar	Vet inte
ACE/ARB					
Betablockerare					
Statiner					
Calciumblockerare					
Diuretika					
Långverkande nitrat					
Andra: _____					

Det finns skriftliga delegeringsrutiner för läkemedelstitrering för sjuksköterskorna

☐ Ja

☐ Nej

☐ Vet inte

Sjuksköterskorna korrigerar läkemedelslistor i journalen, t.ex. efter justering, rätta till felaktiga doseringar, dubbletter etc.

☐ Ja

☐ Nej

☐ Vet inte

Alla patienter får minst ett läkarbesök under sin uppföljning vid hjärtrehabiliteringsenheten.

☐ Ja

☐ Nej

☐ Vet inte

Vilka läkare sköter återbesöken efter hjärtinfarkt? Skatta fördelningen i procent.

Överläkare/specialistläkare _____%

ST läkare i kardiologi _____%

Randande ST läkare _____%

Vikarierande _____%

AT läkare _____%

Vet inte ☐

Hur många timmar i genomsnitt träffar varje patient följande professioner i hjärtrehabiliteringsteamet under det första året, dvs till och med andra SEPHIA besöket (enskilda samtal, ej grupper)?

	Antal timmar totalt	Hur många enskilda besök	Ej tilläpligt
Sjuksköterska			
Sjukgymnast/fysioterapeut			
Läkare			
Psykolog/kurator			
Dietist			

Har ni möjlighet att remittera patienter till dietist (välj ett eller flera alternativ från listan)?

- ☐ Vi har egen dietist
- ☐ Vi remitterar till dietist på sjukhuset
- ☐ Vi remitterar till dietist inom primärvård
- ☐ Vi remitterar aldrig till dietist
- ☐ Vet ej

Enligt Er uppfattning, hur stor andel av era patienter träffar dietist? ___%,Vet inte☐

Vilken typ av material om kost delas ut till patienterna (välj ett eller flera alternativ från listan)?

- ☐ Tryckt material, industrisponsrad
- ☐ Tryckt material, ej industrisponsrad
- ☐ Eget material
- ☐ Hänvisning till webbsidor, externa eller egna
- ☐ Endast muntliga råd
- ☐ Vet ej

Har någon i följande personalgrupper på hjärtrehabiliteringsenheten har genomgått vidareutbildning i rökavvänjning (formell kurs, inte föreläsning) (välj ett eller flera alternativ från listan)?

- ☐ Sjuksköterskor
- ☐ Sjukgymnaster/fysioterapeuter
- ☐ Läkare
- ☐ Kuratorer/psykologer
- ☐ Annan: _____

☐ Ingen i teamet har gått vidareutbildning i rökavvänjning

☐ Vet ej

Har ni möjlighet att remittera rökare till kvalificerad rådgivning (välj ett eller flera alternativ från listan)?

☐ Nej

☐ Ja, till specialistenhet (rökavvänjningsmottagning eller liknande)

☐ Ja, till primärvård

☐ Vet ej

Rekommenderar ni nikotinersättningsmedel som rökavvänjningsmedel till patienterna (välj ett svar)?

☐ Ja

☐ Nej

☐ Vet ej

Skrivs Champix ut på hjärtrehabiliteringsenheten (välj ett svar)?

☐ Ja

☐ Nej

☐ Vet ej

Patienter erbjuds stresshantering på hjärtrehabiliteringsenheten (välj ett eller flera alternativ från listan):

☐ Stresshantering erbjuds inte

☐ Individualiserad stresshantering på annan enhet inom sjukhuset

☐ Stresshantering i grupp på annan enhet inom sjukhuset

☐ Patienter remitteras till primärvården för stresshantering

☐ Vet ej

☐ Annat: _____

Individualiserad stresshantering vid hjärtrehabiliteringsenheten:

☐ hos sjuksköterska

☐ hos psykolog

☐ hos kurator

☐ Annan, vem:

Stresshantering i grupp på hjärtrehabiliteringsenheten:

- ☐ hos sjuksköterska
- ☐ hos psykolog
- ☐ hos kurator
- ☐ Annan, vem:

Erbjuder ni patientutbildning utöver den utbildning som ges vid enskilda patientbesök (välj ett eller flera alternativ från listan)?

- ☐ Vi har ingen patientutbildning utöver den utbildning som ges vid enskilda patientbesök
- ☐ Interaktiv utbildning i grupp för patienter och närstående, innehållande information om riskfaktorer och hjärtsjukdom (i.e. ”hjärtskola”)
- ☐ Anpassade diskussionsgrupper (ex. utifrån ålder, kön eller diagnos)
- ☐ Patientutbildning ("hjärtskola") på utländska språk för patienter som inte talar svenska
- ☐ Anpassade diskussionsgrupper för patienter som inte talar svenska
- ☐ Egen webbsida
- ☐ Externa webbsidor
- ☐ Hälsoappar
- ☐ Annat:_____

Hur många utbildningstillfällen erbjuds per patient (totalt antal timmar)? _____

Vilka personalgrupper deltar i patientutbildning (välj ett eller flera alternativ från listan)?

- ☐ Läkare
- ☐ Sjuksköterska
- ☐ Sjukgymnast/fysioterapeut
- ☐ Dietist
- ☐ Psykolog
- ☐ Kurator
- ☐ Annan profession, vilken: _____
- ☐ Vet ej

För patienter som inte talar svenska (välj ett eller flera alternativ från listan):

- ☐ Avsätts längre tid för individuella besök till sjuksköterska
- ☐ Avsätts längre tid för individuella besök till läkare
- ☐ Endast professionella tolkar får tolka
- ☐ Anhöriga får tolka
- ☐ Erbjuds skriftligt material om riskfaktorer/levnadsvanor på eget språk
- ☐ Erbjuds skriftligt material om riskfaktorer/levnadsvanor på engelska
- ☐ Annat: _____

Besök till hjärtrehabiliteringsenheten erbjuds utanför ordinarie arbetstid, dvs kvällar och/eller helger

	Endast dagtid (8-16:30)	Även kvällstid (efter 16:30) och/eller helger	Vet inte
Besök till läkare			
Besök till sjuksköterska			
Besök till sjukgymnast/fysioterapeut			
Patientutbildning i grupp (ex hjärtskola)			
Hjärtgympa			

Hur länge behåller sjukhuset vanligen det medicinska ansvaret för patienterna, dvs. efter hur många månader remitteras patienterna ut till läkare inom primärvården/privat vårdgivare för fortsatt uppföljning?

Månader: _____

Om utremittering till primärvård eller privat vårdgivare för fortsatt uppföljning gäller följande (välj ett eller flera alternativ från listan):

- ☐ Formell remiss med generell text skickas
- ☐ Formell remiss med individualiserad text skickas
- ☐ Remisstexten brukar innehålla individanpassade målvärden avseende fortsatt sekundärpreventiv behandling
- ☐ Remisstexten brukar innehålla generella råd avseende sekundärpreventiv behandling eller att dylika råd bifogas remissen på separat papper
- ☐ Läkaren skriver remiss
- ☐ Sjuksköterskan skriver remiss

□ Ingen formell remiss skickas

För patienter som inte kan eller vill delta i sjukhusbaserad hjärtrehabilitering, erbjuder ni andra möjligheter för uppföljning hos läkare och sjuksköterska (frågor avseende sjukgymnastik/träning kommer i separat kapitel) (välj ett eller flera alternativ från listan)?

□ Hembaserad hjärtrehabiltering, som följs upp/monitoreras av hjärtrehabiliteringsteamets personal (innefattar uppföljning via telefon, internet, mobilappar, samt övrig distansmonitorering)

□ Uppföljning hos läkare på vårdcentral

□ Uppföljning hos sjuksköterska på vårdcentral

□ Ingen uppföljning

□ Vet ej

Uppföljningens struktur har ändrats de senaste 12 månaderna.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Om ändringar har gjorts, beskriv gärna vilka:

_____

Fysisk aktivitet och träning

Deltagande i sjukgymnast-/fysioterapeut-ledd träning vid hjärtrehabiliteringsenheten erbjuds följande patienter med hjärtsjukdom (markera alla alternativ som stämmer):

□ Patienter som vårdats för hjärtinfarkt

□ Patienter som vårdats för instabil angina

□ Patienter som vårdats för stabil angina

□ Patienter som har genomgått elektiv CABG

□ Patienter som har genomgått elektiv PCI

□ Stabil kranskärlssjukdom (utan föregående akut händelse, elektiv PCI eller CABG)

□ Patienter med hög risk för kranskärlssjukdom (ex patienter med diabetes, metabola syndromet eller familjär hyperkolesterolemi)

□ Patienter med hjärtsvikt

□ Patienter med hjärtarytmier

□ Patienter som fått pacemaker eller ICD

□ GUCH patienter

□ Patienter som genomgått övrig hjärtkirurgi än CABG

□ Patienter som genomgått hjärttransplantation

□ Patienter med perifer kärlsjukdom

□ Andra: _____

Härefter avser frågorna endast patienter som drabbats av hjärtinfarkt som uppfyller Era kriterier för hjärtrehabilitering.

Patienterna träffar sjukgymnast/fysioterapeut under vårdtiden för att diskutera träningens del i hjärtrehabiliteringen.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Patienterna erbjuds individuellt besök till sjukgymnast/fysioterapeut efter utskrivning.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Patienterna erbjuds uppföljande besök till sjukgymnast/fysioterapeut efter avslutad träning (på sjukhus eller egen hand).

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Vi har tillfredsställande mottagningslokaler för enskilda patientbesök till sjukgymnast/fysioterapeut.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Vi har tillfredsställande lokaler för gruppträning.

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Vi har tillfredsställande utrustning för att bedriva gruppträning (t.ex motionscyklar, hantlar, styrketräningsmaskiner, mattor, musikanläggning etc)

Stämmer inte alls *Stämmer helt* *Vet inte/ Ej aktuellt*

1 2 3 4 5 6 □/□

Patienter erbjuds följande i samband med individuellt besök hos sjukgymnast/fysioterapeut vid vår enhet (markera alla alternativ som erbjuds):

	Första besök	Uppföljande besök	Erbjuds inte
Submaximalt cykeltest utan EKG monitorering			
Submaximalt cykeltest med EKG monitorering			
Maximalt cykeltest utan EKG monitorering			
Maximalt cykeltest med EKG monitorering			
Maximalt cykeltest med EKG monitorering och mätning av syreupptagningsförmåga (CPX cykling)			
6 minuters gångtest			
Muskelfunktionstest (ex axelflexion, tåhävning)			
Utdelning/genomgång av träningsdagbok			
Uppföljning av ifylld träningsdagbok			
Fysisk aktivitet på recept (FaR)			

Patienter erbjuds följande typ av träning (markera alla alternativ som stämmer):

□ Cirkelträning

□ Gympa

□ Styrketräning med maskiner och/eller vikter

□ Bassängträning

□ Spinning

□ Stavgång

□ Medicinsk yoga

□ Annan träning, vad: _____

Hur lång tid brukar träningspasset ta? (inklusive uppvärmning, träning, och nedvarvning/avspänning)? _____ min

Hur många gånger per vecka erbjuds patienten delta i träningen? _____ ggr/vecka

Hur många veckor erbjuds träningen? _____ veckor

Patienter som inte kan eller vill delta i denna träning, erbjuds följande alternativ (markera alla alternativ som stämmer):

- ☐ Hem-baserad träning som följs upp av hjärtrehabiliteringsteamets sjukgymnaster/fysioterapeuter (t.ex besök, telefon, internet, mobilappar, samt övrig distansmonitorering)
- ☐ Hem-baserad träning som inte följs upp av hjärtrehabiliteringsteamets sjukgymnaster/fysioterapeuter
- ☐ FaR eller annan egenträning
- ☐ Remiss till sjukgymnast/fysioterapeut på vårdcentral
- ☐ Patient hänvisas till patientförening (ex Riksförbundet HjärtLung)
- ☐ Inget av ovanstående
- ☐ Vet ej
- ☐ Annat, vad:_____

Markera vilka påstenden nedan som passar bäst in på era patienter som inte talar svenska (markera alla alternativ som stämmer):

- ☐ Avsetts längre tid för individuella besök till sjukgymnast/fysioterapeut
- ☐ Erbjuds delta i träningsgrupper på sjukhuset i tolks närvaro
- ☐ Erbjuds delta i träningsgrupper på sjukhuset utan tolk
- ☐ Erbjuds inte deltagande i träningsgrupper på sjukhuset
- ☐ Erbjuds träningsdagbok på eget språk
- ☐ Erbjud träningsdagbok på engelska
- ☐ Erbjuds annat skriftligt material om fysisk aktivitet/träning på eget språk
- ☐ Erbjuds annat skriftligt material om fysisk aktivitet/träning på engelska
- ☐ Inget av ovanstående
- ☐ Annat: _____

Hur många heltids sjukgymnast/fysioterapeut-tjänster (ex 1,5) finns inom eller tillhör Er hjärtrehabiliteringsenhet som avser omhändertagande av patienter med hjärtinfarkt? _____

Tjänstgör sjukgymnasterna/fysioterapeuterna enbart på hjärtrehabiliteringen eller också på avdelningen (välj ett svar)?

☐ Tjänstgör enbart på hjärtrehabiliteringen

☐ Tjänstgör också på avdelning

☐ Vet inte

Har sjukgymnasterna/fysioterapeuterna har genomgått vidareutbildning i kognitiv beteendeterapi och/eller motiverande samtal (MI) (minimum 2 dagars utbildning)?

Nej, ingen av dem *Ja, alla* *Vet inte*

1 2 3 4 5 6 ☐

Nu är Ni nästan klara!

Allmänna kommentar till hela enkäten:

_____

_____

Vilka har bidragit till information för att svara på detta formulär?

☐ Sjuksköterska

☐ Läkare

☐ Sjukgymnast/fysioterapeut

☐ Psykolog/kurator

☐ Dietist

☐ Annan: _____

Supplementary material 2

A full list of variables included in the OPLS-DA in paper IV.

VARIABLE NAME	DETAILS	TYPE
CR organization variables		
In-hospital work routines		
Liaison with CR physio pre-discharge	Patients have a pre-discharge consult with a CR physiotherapist, to discuss the physical activity and exercise training components of CR	Scale 1-6*
Liaison with CR nurse pre-discharge	Patients have a pre-discharge consult with a CR nurse to discuss the CR programme	Scale 1-6
Discharge consult protocols available	Written protocols are available for the physican´s discharge consult	Yes/no
Discharge letter includes follow-up info	The patients´ discharge letter contains information on the CR follow-up plan (i.e. time of initial assessment, personnel involved in CR and length of follow-up)	Yes/no
Discharge letter includes medication info	The patients´ discharge letter contains information on the patients´ current medical regime	Yes/no
Discharge letter includes lifestyle info	The patients´ discharge letter contains information on lifestyle advice (i.e. diet, smoking cessation, physical activity and exercise)	Yes/no
Discharge letter includes risk factor info	The patients´ discharge letter contains information on CVD risk factors (i.e. therapeutic goals for SBP and LDL-C)	Yes/no
IA scheduled prior to discharge	Initial assessment at the CR centre is scheduled before discharge from hospital	Yes/no
Next of kin attend discharge consult	The patients are encouraged to ask next of kin to attend the discharge consult prior to hospital discharge	Scale 1-6
The CR team and facilities		
Multidisciplinary CR team	The CR centre has a multidisciplinary team consisting of at least nurses, physiotherapists and physicians	Yes/no
Medical director	The CR centre has a medical director	Yes/no
Dietician part of CR team	A dietician is a part of the CR team	Yes/no
Psychologist part of CR team	A psychologist or social worker is a part of the CR team	Yes/no
No of CR nurses/100 patients/year	Number of nurses employed at the CR centre/100 patients/year	Number
No of physios/100 patients/year	Number of physiotherapists employed at the CR centre/100 patients/year	Number
CR nurses - CBT/MI training	CR nurses have recieved formal training in cognitive behavioural therapy and/or motivational interviewing	Scale 1-6
Physios - CBT/MI training	CR physiotherapists have recieved formal training in motivational interviewing and/or cognitive behavioural therapy	Scale 1-6
CR team trained in tobacco counselling	At least one member of the CR team has recieved formal training in tobacco counselling	Yes/no
Patient case meetings	The CR team has regular multidisciplinary team meetings to discuss patient cases	Yes/no
Operational CR team meetings	The CR team has multidisciplinary team meetings to discuss organisational matters and quality improvement	Categorical 1-6
CR nurses adjust antihypertensive meds	The CR nurses independently adjust the dosage of antihypertensive medication	Yes/no
CR nurses adjust lipid-lowering meds	The CR nurses independently adjust the dosage of lipid lowering medication	Yes/no

Protocols for medication adjustment	The CR nurses have written protocols on how to adjust antihypertensive and lipid-lowering medication	Yes/no
Adequate facilities	Self-reported staff satisfaction with facilities used for individual patient follow-up visits and exercise training	Scale 4-24
Self-reported team spirit	Self-reported team spirit of the CR team	Scale 1-6
Staff turnover - nurses	Nursing staff turnover during the last 2 years	Categorical 1-4
Staff turnover - physio	Physiotherapist staff turnover during the last 2 years	Categorical 1-4
Staff turnover - medical director	Medical director position turnover during the last 2 years	Categorical 1-4
Vacancies in CR team	The CR centre has had vacancies during the last year (nurses, physiotherapists or the medical director)	Yes/no
Change in work routines during last year	During the last year patient follow-up and work routines have changed at the CR centre	Scale 1-6
Audit data used for quality improvement	The CR centre uses SWEDEHEART data regularly to improve their own organisation and patient care	Categorical 1-3
University hospital	CR centre is situated at a university hospital	Yes/no
Size of CR centre	Number of MI patients eligible for follow-up at the CR centre, divided into five groups (<50, 51-100, 101-150, 151-200 or >200)	Categorical 1-5
Structure of CR programme		
Start of CR programme (IA) ≤ 3 weeks	The initial assessment with a CR nurse is provided within 3 weeks from hospital discharge	Yes/no
IA: Written individual risk factor goals	During the initial assessment with a CR nurse the patients recieves written information on therapeutic risk factor goals and lifestyle or a written copy of their risk factor values	Yes/no
IA: Diet/nutrition counselling	During the initial assessment with a CR nurse diet/nutritional counselling is provided	Yes/no
IA: Physical activity counselling	During the intial assessent with a CR nurse the patients physical activity counselling is provided	Yes/no
IA: Tobacco counselling	During the intial assessent with a CR nurse tobacco counselling is provided, if appropriate	Yes/no
IA: Alcohol counselling	During the intial assessent with a CR nurse alcohol counselling is provided, if appropriate	Yes/no
IA: Weight control counselling	During the intial assessent with a CR nurse weight and waist circumference are assessed and weight control counselling is provided, if appropriate	Yes/no
IA: BP measured	During the intial assessent with a CR nurse the patient´s blood pressure is measured	Yes/no
IA: Blood lipid assessment	During the intial assessent with a CR nurse the patient´s blood lipids are measured or in-hospital values are assessed	Yes/no
IA: Medication reviewed	During the intial assessent with a CR nurse the patient´s current medical regime is reviewed	Yes/no
IA: Psychosocial management	During the intial assessent with a CR nurse psychosocial health is assessed verbally and the patient is counselled, if appropriate	Yes/no
IA: Psychosocial screening instruments	During the intial assessent with a CR nurse psychosocial health is assessed using validated screeening instruments	Yes/no
IA: Vocational support	During the intial assessent with a CR nurse the patient´s social situation is assessed and vocational support provided, if appropriate	Yes/no
Long-term follow-up of goals	During a subsequent follow-up visits the patients´ risk factor and lifestyle goals are followed-up in a structured way	Scale 1-6

Continuation in CR nurse contact	The patients are followed by the same CR nurse for the whole duration of the CR programme	Scale 1-6
Professional dietary counselling	The CR centre refers patients to professional counselling for unhealthy dietary habits (own dietician, at hospital or in primary care), if appropriate	Yes/no
Written dietary information	The CR centre provides patients with written information on diet and healthy diet choices	Yes/no
Professional tobacco counselling	The CR centre can refer patients to professional counselling for tobacco cessation	Yes/no
Group-based stess management	The CR centre provides group-based stress management or can refer patients to group-based stress management, if appropriate	Yes/no
NRT recommended	The CR centre recommends nicotine replacement therapy for current smokers	Yes/no
Varenicline prescribed	The CR centre physicians prescribe varenicline to current smokers	Yes/no
Need for physician consulation adapted	Patients´ need for a physican consulation during the CR programme is individually evaluated	Yes/no
Digital patient education offered	The CR centre offers patient education to patients via own or extrenal web-site or via web-applications	Yes/no
Interactive patient education offered	The CR centre offers interactive group-based patient education (heart school) as a part of the comprehensive CR programme	Yes/no
Hours spent with nurse or physician	The number of hours each patient on average spends with a CR nurse and/or physician during the follow-up period	Number
Relatives encouraged to attend CR visits	Patients are encouraged to bring a family member to their follow-up visits	Scale 1-6
Extended opening hours at CR centre	The CR centre offers services (cardiologist-, nurse-, or physiotherapist consulatation, group education, group training, etc.) outside office hours	Yes/no
Home-based CR available	Home-based CR is offered to patient who cannot or are unwilling to take part in centre-based CR	Yes/no
Duration of CR programme	Duration of CR programme (months), i.e. time between referral and when patients are referred to primary care	Months
CR centre uptake 2016	Proportion of eligible patients (<75 years of age discharged alive with MI diagnosis) who attended 1-year close-out visit at CR centre in 2016	Proportion
Exercise-based cardiac rehabilitation		
1st physio visit (pre exCR assessment)	Patients are offered an initial pre exCR visit to a physiotherapist	Yes/no
1st physio visit: ex test performed	The patients perform an symptom-limited exercise test during the initial visit with a physiotherapist	Yes/no
1st physio visit: muscle function test	The patients perform muscle function tests during the initial visit with a physiotherapist	Yes/no
1st physio visit: ex log provided	During the initial visit with a physiotherapist the patients are provided with an exercise log, to register their physical activity and exercise activities	Yes/no
2nd physio visit (close-out post exCR)	Patients are offered a follow-up (close-out) visit with a physiotherapist post exCR attendance	Yes/no
2nd physio visit: ex test performed	The patients perform a symptom-limited exercise test during the follow-up visit with a physiotherapist	Yes/no
2nd physio visit: muscle function test	The patients perform muscle function tests during the follow-up visit with a physiotherapist	Yes/no
2nd physio visit: ex log reviewed	During the follow-up visit with a physiotherapist the patients exercise log is evaluated	Yes/no

Different forms of exCR available	The number of different kinds of exercise training modalities (combination of strength and required) offered to patients	Number
Home-based exCR is available	Home-based exCR is offered to patient who are unable or unwilling to take part in centre-based exCR	Yes/no
Duration of exCR programme	The average duration of centre-based, supervised, exCR programme offered to patients	Time (min)
Patient-level variables		
Age	Age at the time of MI	Years
Gender	Gender	Male/female
Country of birth (128)	Born in Sweden, Nordic countries other than Sweden, Europe outside of Nordic countries or outside of Europe	Categorical 1-4
Occupation (128, 178)	Occupational level classified as high/intermediate level salaried employees, assistant non-manual employees, skilled workers, unskilled workers, self-employed (including farmers) or other	Categorical 1-6
Marital status (128)	Living with a partner or living alone	Dicotomized
Highest education (128)	Education stratified into three levels according to the highest attained level: under 10 years (compulsory school only), 10 to 12 years (upper school) and, over 12 years (college/university level).	Categorical 1-3
Disposable income (128)	Household disposable income (SEK) is an individualized weighted average income i.e., the sum of the family members' disposable income multiplied by the individual consumption weights and divided by their aggregate consumption weight.	Quintiles
Systolic BP at baseline	Systolic blood pressure at MI admission	mmHg
BMI at baseline	Body mass index at MI admission	kg/m2
LDL-C at baseline	LDL-C during MI hospitalization	mmol/L
Smoking status at baseline	Active smoker at MI admission	Categorical 1-3
Prior history of CVD	Prior history of MI, PCI, CABG or stroke at MI admission	Yes/no
Prior history of DM	Prior history of diabetes mellitus at MI admission	Yes/no
Prior history of hypertension	Prior history of hypertension at MI admission	Yes/no
LVEF during admission	Left ventricular ejection fraction during admission	Categorical 1-4
Discharge meds: Platelet inhibitor	Platelet inhibitors prescribed at discharge	Yes/no
Discharge meds: ACEi/ARB	ACE inhibitors or ARBs prescribed at discharge	Yes/no
Discharge meds: LLT	Lipid lowering treatment (statin, ezetimibe or other LLT) prescribed at discharge	Yes/no
Discharge meds: beta blockers	Beta blockers prescribed at discharge	Yes/no
Other serious disease	Other serious disease prior to admission (i.e. dementia, terminal cancer)	Yes/no
Type of MI	Type of MI (STEMI or NSTEMI)	Categorical 1-2
Participated in group education during CR	Patient participated in interactive group-based patient education (heart school) as a part of the CR programme	Yes/no
Participated in stress mangament during CR	Patient participated in group-based stress management as a part of the CR programme	Yes/no
Professional tobacco counselling during CR	Patient received professional tobacco counselling as a part of the CR programme	Yes/no

Distance between home and CR centre	Driving distance between patient´s home and the CR centre	km

*1=totally disagree, 6=totally agree CBT/MI, cognitive behavioural training/motivational interviewing; CR, cardiac rehabilitation; DM, diabetes mellitus; exCR, exercise-based cardiac rehabilitation; IA, initial assessment; LLT, lipid lowering treatment; MI, myocardial infarction; OGTT, oral glucose tolerance test; physio, physiotherapist; No, number

Supplementary material 3

THE PERFECT CR INDEX

Discharge

1. The patient receives written information or is directed to a local webpage for information on the structure of the follow-up.
2. The patient receives written information or is directed to a local webpage for information on goals for lifestyle changes AND risk factors. Both must be fulfilled.

The cardiac rehabilitation team

3. A nurse, physician and physiotherapist are a part of the team, either employed at the cardiac rehabilitation centre or other clinic/hospital-unit.
4. The team is as above AND the centre has a medical director: additional half point.

Facilities

5. Average score for facilities (for individual follow-up visits with a nurse, physician, and physiotherapist, and for group sessions) 4.0–5.0 and no score ≤3
6. Average score: 5.1–6.0 and no score ≤3

Patient assessment and follow-up

7. First assessment with a nurse is ≤3 weeks from discharge.
8. The cardiac rehabilitation programme has no age limit.
9. The patient receives written information on risk factors and lifestyle changes OR a written copy of their values AND the therapeutic goals are followed up.

Diet

10. Assessment and counselling of diet is performed at first assessment with a nurse, referral to dietician is possible and written material is handed out.
11. The cardiac rehabilitation centre has its own dietician.

Tobacco

12. Assessment of smoking status and abstinence is recommended during first assessment with a nurse.

13. Referral to qualified counselling for smoking cessation is available AND/OR staff has training in aiding in smoking cessation.

Blood pressure

14. Blood pressure measurement is performed during first assessment with a nurse.

15. Nurses may, independently, adjust dosage of blood pressure medication (at least ACE-blockers and betablockers).

Weight

16. Weight and waist circumference are measured at first assessment with a nurse.

17. Counselling of weight loss for overweight is performed.

Blood lipids

18. Blood lipids are measured, or in-hospital values are evaluated at first assessment with a nurse.

19. Nurses may, independently, adjust dosage of stains.

Mental health

20. Oral (informal) or structured assessment of mental health is performed AND an assessment of social situation is performed at the first assessment with a nurse.

21. The cardiac rehabilitation centre has its own psychologist/social worker OR group-based stress management is available on location or on referral.

Medication

22. Medical regime is reviewed at first assessment with a nurse.

Rounds and team meetings

23. The team has regular rounds to discuss patient cases.

24. The team has regular meetings to discuss operational matters.

Patient education

25. Patient education is available in the form of local webpage or health-applications.

26. Patient education is available in the form of interactive group education or group education adapted for patient needs.

Physiotherapy/exercise training

27. Patients meet with a physiotherapist before discharge from hospital AND are offered an initial follow-up visit with a physiotherapist post-discharge.

28. Patients are offered participation in centra-based exercise training AND a follow-up visit with a physiotherapist.

29. For extra half point: Both of the above AND the centre offers patients at least 24 training sessions.

Quality registry

30. The cardiac rehabilitation centres use SEPHIA data for own quality control and operational improvements.

Supplementary material 4

VIP-and loading values for meaningful variables (VIP >0.8 and CI not including zero) for the prediction of LDL-cholesterol (<1.8 mmol/L) at one-year post-MI.

Variable name	VIP value	Standard error (SE)	Loading value	Standard error (SE)
In-hospital work routines				
Discharge consult protocols available	1.74	0.28	0.05	0.01
Discharge letter includes risk factor info	1.04	0.40	0.03	0.01
Discharge letter includes lifestyle info	0.80	0.19	0.02	0.01
The CR team and facilities				
Medical director	1.71	0.26	0.05	0.01
Psychologist part of CR team	1.59	0.31	0.04	0.01
Protocols for medication adjustment	1.58	0.23	0.04	0.01
CR nurses adjust lipid-lowering meds	1.55	0.37	0.04	0.01
Adequate facilities	1.55	0.49	0.04	0.01
University hospital	1.43	0.34	0.04	0.01
Operational CR team meetings	1.36	0.28	0.04	0.01
Patient case meetings	1.27	0.45	0.04	0.01
Self-reported team spirit	1.21	0.36	0.03	0.01
CR nurses - CBT/MI training	1.13	0.22	0.03	0.01
Audit data used for quality improvement	1.00	0.20	0.03	0.01
No of physios/100 patients/year	0.96	0.55	0.01	0.01
Structure of CR programme				
Extended opening hours at CR centre	2.17	0.23	0.06	0.01
IA: Psychosocial management	2.09	0.39	0.06	0.01
Continuation in CR nurse contact	1.75	0.32	0.05	0.01
Need for physician consult adapted	1.74	0.33	0.05	0.01
CR centre uptake 2016	1.66	0.24	0.05	0.01
IA: Psychosocial screening instruments	1.33	0.33	0.04	0.01
Long-term follow-up of goals	1.27	0.19	0.04	0.01
IA: Alcohol counselling	0.91	0.15	0.03	0.00
Duration of CR programme	0.91	0.36	0.03	0.01
IA: Vocational support	0.81	0.28	0.02	0.01
Exercise-based CR				
1st physio visit: ex test performed	1.83	0.45	0.05	0.01
1st physio visit (pre exCR assessment)	1.50	0.28	0.04	0.01
1st physio visit: ex log provided	1.36	0.41	0.04	0.01
Different forms of exCR available	1.28	0.69	0.04	0.02

2nd physio visit (close-out post exCR)	1.27	0.21	0.04	0.01
2nd physio visit: ex test performed	1.09	0.27	0.03	0.01
1st physio visit: muscle function test	1.02	0.64	0.03	0.02
Home-based exCR is available	0.92	0.32	0.03	0.01
Patient-related variables				
Participated in ex training during CR	1.60	0.77	0.05	0.03
Male gender	1.57	0.65	0.05	0.02
Discharge meds: LLT	1.48	0.52	0.05	0.02
Prior history of DM	1.37	0.31	0.05	0.01
Discharge meds: ACEi/ARB	1.36	0.51	0.05	0.02
Participated in group education during CR	1.21	0.62	0.04	0.02
Previous smoker at baseline	0.99	0.31	0.03	0.01
Discharge meds: Platelet inhibitor	0.93	0.54	0.03	0.02
Prior history of hypertension	0.91	0.52	0.03	0.02
Negative predictors				
LDL-C at baseline	3.90	0.66	-0.13	0.03
Physios - CBT/MI training	1.09	0.39	-0.03	0.01
IA: Diet/nutrition counselling	1.06	0.76	-0.03	0.02
IA: Physical activity counselling	1.04	0.70	-0.03	0.02
Active smoker at baseline	0.86	0.29	-0.03	0.01

CR, cardiac rehabilitation; CBT/MI, cognitive behavioural training/motivational interviewing; No, number; physio, physiotherapist; IA, initial assessment; ex, exercise; exCR, exercise-based cardiac rehabilitation; LLT, lipid lowering treatment; DM, diabetes mellitus; AECi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blockers; LDL-C, low-denisity lipoprotein cholesterol.

Supplementary material 5

VIP-and loading values for meaningful variables (VIP >0.8 and CI not including zero) for the prediction of BP (<140/90 mmHg) at one-year post-MI.

Variable name	VIP value	Standard error (SE)	Loading value	Standard error (SE)
In-hospital work routines				
Discharge consult protocols available	1.60	0.36	0.05	0.01
Discharge letter includes risk factor info	1.42	0.39	0.05	0.01
Discharge letter includes lifestyle info	1.16	0.37	0.04	0.01
IA scheduled prior to discharge	0.86	0.43	0.03	0.01
The CR team and facilities				
Psychologist part of CR team	2.00	0.54	0.07	0.02
Adequate facilities	1.96	0.32	0.06	0.01
Protocols for medication adjustment	1.56	0.52	0.05	0.02
Medical director	1.47	0.40	0.05	0.01
Operational CR team meetings	1.34	0.36	0.04	0.01
CR nurses - CBT/MI training	1.31	0.34	0.04	0.01
Audit data used for quality improvement	1.27	0.29	0.04	0.01
No of physios/100 patients/year	1.24	0.35	0.04	0.01
Self-reported team spirit	1.19	0.31	0.04	0.01
Multidisciplinary CR team	1.16	0.42	0.04	0.01
CR nurses adjust lipid-lowering meds	1.07	0.37	0.03	0.01
University hospital	0.98	0.15	0.03	0.01
Change in work routines during last year	0.87	0.38	0.03	0.01
Structure of CR programme				
IA: Psychosocial management	2.34	0.44	0.08	0.01
CR centre coverage 2016	1.78	0.23	0.06	0.01
Extended opening hours at CR centre	1.51	0.48	0.05	0.02
Continuity in CR nurse-patient contact	1.31	0.35	0.04	0.01
IA: Psychosocial screening instruments	1.25	0.44	0.04	0.02
IA: Alcohol counselling	1.22	0.56	0.04	0.02
Long-term follow-up of goals	1.14	0.37	0.04	0.01
Need for physician consult adapted	1.01	0.45	0.03	0.02
Exercise-based CR				
1st physio visit: ex test performed	1.88	0.59	0.06	0.02
Different forms of exCR available	1.77	0.34	0.06	0.01
1st physio visit (pre exCR assessment)	1.46	0.45	0.05	0.01
Duration of ex training programme	1.40	0.28	0.05	0.01
1st physio visit: muscle function test	1.27	0.62	0.04	0.02

1st physio visit: ex log provided	1.19	0.50	0.04	0.02
2nd physio visit: ex test performed	1.18	0.51	0.04	0.02
2nd physio visit (close-out post exCR)	1.02	0.47	0.03	0.01
Home-based exCR is available	1.02	0.56	0.03	0.02
2nd physio visit: muscle function test	0.88	0.62	0.03	0.02
Patient-related variables				
Participated in exCR	1.50	0.36	0.07	0.02
Type of MI (STEMI)	1.36	0.29	0.07	0.01
Disposable income	1.30	0.26	0.06	0.01
Participated in group education	1.11	0.15	0.05	0.01
Male gender	1.07	0.38	0.05	0.02
Educational level	0.93	0.20	0.04	0.01
Living with a partner	0.91	0.26	0.04	0.01
LDL-C at baseline	0.80	0.20	0.04	0.01
Negative predictors				
Prior history of hypertension	2.93	0.19	-0.14	0.01
Prior history of DM	1.66	0.40	-0.08	0.02
Systolic BP at baseline	1.36	0.25	-0.07	0.01
Age	1.18	0.24	-0.06	0.01
BMI at baseline	1.10	0.19	-0.06	0.01
Prior history of CVD	1.10	0.36	-0.06	0.02
Discharge meds: ACEi/ARB	0.88	0.47	-0.04	0.02

IA, initial assessment; CR, cardiac rehabilitation; CBT/MI, cognitive behavioural training/motivational interviewing; No, number; physio, physiotherapist; ex, exercise; exCR, exercise-based cardiac rehabilitation; MI, myocardial infarction; STEMI, ST-elevation myocardial infarction; LDL-C, low-denisity lipoprotein cholesterol; DM, diabetes mellitus; BP, blood pressure; BMI, body mass index; CVD, cardiovascular disease; AECi, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blockers.

Supplementary material 6

VIP-and loading values for meaningful variables (VIP >0.8 and CI not including zero) for the prediction of smoking abstinence (yes/no) at one-year post-MI.

Variable name	VIP value	Standard error (SE)	Loadings value	Standard error (SE)
The CR team and facilities				
Psychologist part of CR team	1.69	0.66	0.05	0.02
Change in work routines during last year	1.57	1.45	0.04	0.04
Structure of CR programme				
Varenicline prescribed	1.98	1.85	0.06	0.05
Group-based stress management	1.69	0.83	0.05	0.02
Hours spent with nurse or physician	1.24	0.79	0.03	0.02
Patient-related variables				
Participated in exCR	2.51	0.27	0.18	0.02
Participated in group education	1.97	0.29	0.14	0.02
Disposable income	1.67	0.39	0.12	0.03
Living with a partner	1.47	0.63	0.10	0.04
LDL-C at baseline	0.96	0.21	0.07	0.01
Education	0.80	0.32	0.06	0.02
Negative predictors				
Prior history of CVD	2.06	0.26	-0.15	0.02
Prior history of DM	1.22	0.39	-0.09	0.03
Prior history of hypertension	0.96	0.35	-0.07	0.02
Age	0.86	0.34	-0.06	0.02

CR, cardiac rehabilitation; ex, exercise; exCR, exercise-based cardiac rehabilitation; LDL-C, low-denisity lipoprotein cholesterol; CVD, cardiovascular disease; DM, diabetes mellitus.

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"while probabilities encode our beliefs about a static world, causality tells us whether and how probabilities change when the world changes, be it by intervention or by act of imagination."

– Judea Pearl, The Book of Why: The New Science of Cause and Effect

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